INTRA- AND INTER-INDIVIDUAL VARIABILITY IN SLEEP: ASSOCIATIONS WITH NEGATIVE AFFECT AND SYMPATHO-ADRENAL MEDULLARY ACTIVITY

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The majority of sleep research in adults has emphasized inter-individual, as opposed to intra-individual differences, in dimensions of sleep. The current study quantifies individual variability in actigraphy-measured sleep duration and fragmentation and describes the sociodemographic and psychosocial correlates of such variability in a sample of Black and White adults. It then examines the unique associations of average sleep duration, average sleep fragmentation, and individual variability in these parameters with negative affect and nocturnal sympatho-adrenal medullary activity as indexed by catecholamine levels. The sample included 187 adults (53% men; 41% Black; mean age 59.6 years) who wore a wrist actigraph for nine nights and completed well-validated measures of depressive symptoms, anxiety, and hostility. Overnight urinary catecholamine levels were collected over two 15-hour periods. Estimates of within-individual variability in both sleep duration and fragmentation exceeded between-individual differences, and women and Blacks had more individual variability in sleep duration and fragmentation, respectively. In linear regression models, increased variability in sleep parameters was related to reports of stressful life events and a global measure of sleep quality, independent of average sleep parameters. No associations between sleep parameters and negative affect or catecholamine levels were observed, with the exception of a relationship between increased sleep fragmentation and higher nocturnal levels of norepinephrine.

Interactive effects between sleep and negative affect were apparent, such that short and variable sleep were related to higher nocturnal levels of catecholamines only among individuals who were high in negative mood. These findings show that substantial intra-individual variability in sleep exists and suggest that nightly variability may represent an important avenue for future sleep research.

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1.0 INTRODUCTION

Voluntary curtailment of sleep is becoming increasingly common, as the average proportion of individuals sleeping fewer than seven hours per night has increased from 16% to 37% over the past 40 years (National Sleep Foundation, 2002). Additionally, an estimated one third of the U.S. adult population reports frequent nighttime awakenings (National Sleep Foundation, 2005). While it is known that the overall trend in sleep length is declining, a relatively neglected concept in sleep research is the degree of stability within individuals' sleep patterns. For example, few studies have reported whether adults' bed times and sleep durations are consistent from night to night, and it is unknown whether disturbed, fragmented sleep tends to occur regularly or on a more variable basis. Moreover, while the demographic and lifestyle factors that are associated with average sleep parameters have been studied extensively (e.g., Foster & Peters, 1999; O'Connor & Youngstedt, 1995; Zhang, Samet, Caffo, & Punjabi, 2006), the correlates of intra-individual variation in sleep are poorly understood.

Growing evidence suggests that dimensions of sleep are associated with, and perhaps risk factors for, psychological distress. For example, short and fragmented sleep as measured by actigraphy or polysomnography (PSG) are observed among individuals with affective and anxiety-related disorders (Armitage, Trivedi, Hoffmann, & Rush, 1997; Fuller, Waters, Binks, & Anderson, 1997; Korszun et al., 2002; Lemke, Puhl, & Broderick, 1999), and sleep deprivation causes increases in negative affect in healthy populations (Caldwell, Caldwell, Brown, & Smith,

2004; Kahn-Greene, Killgore, Kamimori, Balkin, & Killgore, 2007). However, our understanding of the association between naturally occurring sleep durations and more normative variation in mood remains limited, as studies in non-clinical and non-experimental samples have produced mixed results (National Sleep Foundation, 2002; Jean-Louis, Kripke, & Ancoli-Israel, 2000; Pilcher, Ginter, & Sadowsky, 1997; Totterdell, Reynolds, Parkinson, & Briner, 1994). Additionally, the extent to which stability in sleep-wake patterns are associated with negative affect has not received much attention, despite reports that such intra-individual variability may plan an equally important role in psychological health (Fuligni & Hardway, 2006; Wolfson & Carskadon, 1998).

Short, poor sleep is not only associated with mood, but physical health as well. An increasing body of literature highlights the role of sleep duration and continuity in a number of diseases, including cardiovascular disease (Ayas et al., 2003). While the pathways linking sleep and morbidity are largely unknown, it has been hypothesized that nighttime elevation of the sympatho-adrenal medullary (SAM) axis may be one mechanism by which short or fragmented sleep is associated with an increased risk for cardiovascular disease. Limited data show that restricted and disturbed sleep are indeed related to increased nocturnal catecholamine levels in experimental paradigms or unique populations (Irwin et al., 1999; Irwin, Clark, Kennedy, Gillin, & Ziegler, 2003; Mausbach et al., 2006), but the degree to which sleep coincides with SAM activity under more normative conditions is uncertain. In addition, the effects of intra-individual sleep variability on physiological parameters have not been examined in community samples.

The foremost purpose of the proposed study is to gain a clearer understanding of variability in sleep patterns within a sample of Black and White adults. Intra-individual variability in sleep duration and fragmentation will be characterized, and a number of

demographic, lifestyle, and behavioral factors will be examined as potential correlates of this variability. The proposed study then goes on to assess the unique contributions of average sleep parameters (duration and fragmentation) and variability in these same parameters (duration and fragmentation) to negative affect and nocturnal SAM activity, as characterized by catecholamine levels. Finally, despite the fact that both sleep and negative affect have been linked to increased SAM activity, few studies have considered both of these factors when investigating catecholamine excretion. Therefore, the interaction between negative affect and sleep also will be examined for its association with nocturnal catecholamine levels.

The proposed study has several important implications, including an improved understanding of how short and fragmented sleep are associated with affect and SAM activity in everyday life. A relatively neglected aspect of sleep – variability across nights – is also incorporated to determine whether it too plays a relevant role in psychological and physiological functioning, over and above average sleep parameters. Treatments for sleep disorders often recommend adherence to a strict sleep schedule (Kupfer & Reynolds, 1997; Summers, Crisostomo & Stepanski, 2006) and intervention studies have shown that increasing the stability of sleep patterns leads to improved sleep quality and less daytime sleepiness (Manber, Bootzin, Acebo, & Carskadon, 1996). Positive associations between individual variability in sleep, negative affect, and SAM activity will offer preliminary support that the benefits of regular sleep may extend beyond improved sleep quality.

2.0 LITERATURE REVIEW

2.1 SLEEP DURATION

A substantial amount of research has quantified typical sleep parameters of adults in the United States. In the 2005 Sleep in America poll, adults reported an average of 6.9 hours of sleep per night (National Sleep Foundation), and a 2004 meta-analysis of 65 studies found average sleep duration to range from 5.4 hours to 7.8 hours in 35 to 60-year olds (Ohayon, Carskadon, Guilleminault, & Vitiello, 2004, in Lauderdale et al., 2006). Other large-scale studies have observed mean sleep durations between 5.5 and 6.5 hours when using actigraphy or polysomnography (PSG) (Lauderdale et al., 2006; Redline et al., 2004). These estimates of sleep vary by sex and race. Specifically, both men and Blacks tend to have shorter and less efficient sleep, as measured by actigraphy and PSG, than women and Whites (Goel, Kim, & Lao, 2005; Lauderdale et al., 2006; Ohayon et al., 2004). The consequences of short sleep extend beyond feelings of daytime tiredness, as increasing evidence suggests that sleep duration and fragmentation play a role in both psychological and physical health (see below).

2.2 VARIABILITY IN SLEEP

In addition to average sleep duration and fragmentation, another aspect of sleep that may differ between individuals is variability, or the degree to which sleep varies from night to night. In some individuals, changes in the duration or continuity of sleep may occur on a continuous basis. For example, in a recent study by Knutson, Rathouz, Yan, Liu, and Lauderdale (2007), adults' time in bed and time spent asleep varied by more than an hour over three nights. Sleep latency and sleep efficiency varied by 30 minutes and 8%, respectively. For each sleep parameter, the amount of intra-individual variability exceeded the amount of variability between individuals. Van Hilten et al. (1993) reported considerable intra-individual variability in actigraphy-measured activity and immobility measures across six nights in healthy adults. The authors noted that these differences were not due to first-night or day of the week effects and that women had greater variability in these indices than men. These studies suggest that using "averages" of sleep duration may be ignoring an important aspect of sleep: intra-individual variability.

At least two other studies examined the stability of sleep patterns over time. The first found an increase in self-reported sleep duration over a university semester in college students (Pilcher & Ott, 1998), while the other found a decrease in self-reported time in bed over a comparable period (Hawkins & Shaw, 1992). Although these results suggest that sleep patterns do not remain stable over several months, they do not address sleep changes on a nightly basis. Moreover, they are based upon samples of college students, a population in which regular sleep schedules are traditionally difficult to maintain (Brown, Buboltz, & Soper, 2002).

With the exception of the above studies, little else is known about the stability of adults' sleep from night to night. For one, the correlates of sleep variability have not been described. As estimates of sleep duration tend to differ by race and sex, it is possible that sleep variability

differs between these groups as well. Indeed, Knutson et al. (2007) reported that although race differences in their sample were inconsistent, Whites generally tended to have more stable sleep patterns than Blacks. As previously noted, women also have been found to have more instability in movement and activity across nights than men (Van Hilten et al., 1993). Moreover, a number of lifestyle factors that have been associated with sleep duration, such as stressful life events, health behaviors, or physical health status, may also be correlated with increased variability in sleep patterns; however, these relationships have not been explored to date.

Quantifying variability in sleep may be important for a number of reasons. First, limited research in this area suggests that one night of sleep measurement may not accurately represent typical sleeping patterns. If this is the case, conclusions regarding associations between sleep and other parameters, such as mood or health, may be weaker or even erroneous when based upon one night of assessment. Additionally, although means provide a simplified and well-balanced representation of multiple data points, information may be lost when using averages. For example, means may contain a large amount of within-group heterogeneity. Consider two people who both average 8 hours of sleep every night; however, Person A sleeps 8 hours consistently every night, while Person B sleeps 11 hours one night and 5 hours the next. Although mean sleep duration is identical, these two sleeping patterns are quite different and may have different implications for daytime functioning and health. In the following section, the literature that has linked average sleep duration and fragmentation to psychological health is first reviewed. The possibility that sleep variability may be an additionally important factor in psychological well-being is then introduced.

2.3 SLEEP AND NEGATIVE AFFECT

2.3.1 Sleep Duration and Negative Affect.

One of the most frequently studied psychological correlates of short and fragmented sleep is negative affect. A recent study reported that 56 hours of continual wakefulness results in increased depression, anxiety, and paranoia among healthy adults (Kahn-Greene et al., 2007), and similar decrements in mood have been observed after 37 hours of wakefulness in a small study of military pilots (Caldwell et al., 2004). At least two experimental studies have limited individuals' sleep (four to five hours per night) for either one week (Dinges et al., 1997) or 12 days (Haack & Mullington, 2005), resulting in increased fatigue, confusion, and tension, and decreased optimism-sociability, respectively. However, not all partial sleep deprivation experiments have produced similar results, as an earlier study found that restricting sleep to five and a half hours a night for 60 days did not lead to changes in mood (Webb & Agnew, 1974). Moreover, although participants initially reported increased levels of daytime drowsiness, these effects did not persist throughout the duration of the study, suggesting some degree of adaptation to decreased sleep.

The effects of sleep deprivation studies may be confounded by other factors, such as a lack of social contact or heightened stress. Furthermore, total sleep deprivation represents an extreme behavior that rarely occurs in natural settings. The extent to which average sleep duration and mood are correlated in non-experimental studies is less clear. The 2002 Sleep in America poll found that adults who report sleeping less than six hours per night also report higher levels of anger and sadness and lower levels of optimism and life satisfaction (National Sleep Foundation, 2002). A study of medical residents showed that working continuous hours

without sleep leads to increased negative emotional experiences on the job (Zohar, Tzischinsky, Epstein, & Lavie, 2005). However, at least three other studies have reported null findings regarding sleep duration and measures of well-being and mood (Jean-Louis, et al., 2000; Pilcher, et al., 1997; Totterdell, et al., 1994). In sum, while experimental studies of total and partial sleep deprivation suggest a regulatory role of sleep in affective processes, the findings regarding sleep duration and negative affect in community samples have been mixed.

2.3.2 Sleep Fragmentation and Affect.

Associations between fragmented sleep and negative affect have been studied predominantly within clinical populations. Patients with major depressive disorder have higher levels of nighttime activity and poorer sleep efficiency as measured by actigraphy than non-depressed individuals (Korszun et al., 2002; Lemke et al., 1999). PSG-measured sleep disturbances are common in both depressive disorders and anxiety disorders free from co-morbidities (Armitage et al., 1997; Fuller et al., 1997; Kupfer, 1995). Evidence from non-clinical samples has relied largely on self-reports of sleep disturbances and mood. For example, one study reported that increased negative affect during the day predicts self-reported sleep disturbances on the subsequent night (Brissette & Cohen, 2002), while another found that heightened anxiety results in sleeping difficulties (Moffitt, Kalucy, Kalucy, Baum, & Cooke, 1991). A limitation of these findings is the possibility that levels of negative affect influence perceptions of sleep; however, these studies raise the important point that the relationship between sleep disturbances and mood is thought to be bi-directional (e.g., Buysse, 2004). In sum, while it is plausible that objectively measured sleep fragmentation may be associated with more normative decrements in mood, this relationship has not received much attention outside of psychiatric populations.

2.3.3 Sleep Variability and Affect.

Limited evidence suggests that similar to sleep duration and fragmentation, variability in sleep may also be associated with psychological health. The strongest support for a relationship between sleep variability and negative affect comes from the child and adolescent literature. Several studies have observed links between irregular sleep-wake schedules and negative mood in adolescents. For instance, Fuligni and Hardway (2006) found that more intra-individual variability in total sleep time over 14 nights was related to increased anxiety, depression, and fatigue in a multi-ethnic sample of over 750 adolescents. Moreover, this association was independent of overall sleep duration. Wolfson and Carskadon (1998) reported that adolescents who had large weekend delays in their bedtimes as compared to weekdays were more likely to report daytime sleepiness, behavior problems, and in females only, depressed mood. Relationships between unstable sleep patterns and other behavioral difficulties, such as attention-deficit/hyperactivity disorder, academic difficulty, and poor school functioning, have been observed in school-aged children (Acebo & Carskadon, 2002; Bates, Viken, Alexander, Beyers, & Stockton, 2002; Gruber, Sadeh, & Raviv, 1999).

Only a handful of studies have examined the correlates of sleep variability in older populations. In 1979, Taub and Hawkins characterized college men as regular or irregular sleepers based on self-reported stability of bed times, wake times, and sleep duration. They found that those who maintained regular sleep schedules scored higher on personality measures of dominance, sociability, self-acceptance, self-control, achievement, and intellectual efficiency as compared to men who reported unstable bedtimes and sleep durations. In a small sample of medical students, unstable sleep onset times (as measured by their standard deviations) were related to poor subjective sleep quality as well as poor academic performance (Medeiros,

Mendes, Lima, & Araújo, 2001). Neither of the above studies specified whether the observed associations were independent of average sleep duration. Therefore, while preliminary data suggest that sleep variability is associated with personality traits and academic performance, it is unclear if these links are confounded by other variables. In addition, these studies did not examine associations between sleep patterns and mood *per se*.

Indirect evidence suggesting that sleep variability influences mood can be found in an early experiment conducted by Taub and Berger (1974). In this study, the sleep of 10 "stable" sleepers was shifted so that it occurred over four different time periods in the circadian rhythm (e.g., 8 p.m. to 4 a.m.; 2 to 10 a.m). The shifted sleep conditions resulted in impaired performance on vigilance and calculation tasks as well as increased reports of negative affect compared to the control condition (12 – 8 a.m.). Importantly, the authors note that changes in performance and mood were independent of sleep duration and changes in sleep parameters, suggesting that the timing of sleep was the catalyst for the observed effects. While this experiment does not address variability directly, it suggests that altering the time period over which sleep occurs can lead to changes in affect.

2.3.4 Circadian Rhythm Disruptions and Major Depressive Disorder.

As stated previously, depression is associated with sleep complaints as well as a number of PSG abnormalities (Armitage et al., 1997; Ford & Kamerow, 1989; Kupfer, 1995). Sleep deprivation experiments result in antidepressant effects (Wirz-Justice & Van den Hoofdakker, 1999), and there is some evidence that social circadian rhythms are disrupted prior to or during depressive episodes (Szuba, Yager, Guze, Allen, & Baxter, 1992). In the aggregate, these studies provide evidence of dysregulated circadian rhythms in individuals with major depressive disorder.

Several theories have been proposed as explanations of this phenomenon, including the phase advance model, a deficiency in the build-up of the homeostatic need for sleep (Process S), and an instability or increased variability in circadian rhythms. Although a review of these theories is beyond the scope of this report, it should be noted that circadian disturbances in several physiological functions, including the sleep-wake system, have been repeatedly documented in depressive and other affective disorders. The extent to which these associations are present in non-clinical populations has not received much attention and is one aim of the current proposal.

2.4 SLEEP & NEGATIVE AFFECT: SUMMARY AND LIMITATIONS

Although increasing evidence suggests that both short and fragmented sleep may play a role in psychological health, a number of questions regarding these associations remain. For instance, while experimental sleep deprivation leads to increases in negative affect, the degree to which a short sleep duration is associated with affect outside of experimental conditions is unclear. Increased movement during the night and decreased sleep efficiency are common in depressive and anxiety disorders; however these associations have been studied less frequently using objective measures in community samples free from psychiatric illness.

Links between irregular sleep and mood may also exist, but the available literature on these associations is limited. In particular, while several studies report that irregular sleep-wake schedules are correlated with depression and anxiety in adolescents, it is possible that this association is limited to specific developmental periods. One study that examined sleep variability and mood in adults was Taub and Berger's (1974) experimental work. Although the experimental nature of that study was advantageous in terms of isolating and manipulating the

timing of sleep, the application of these findings to more normative situations is difficult. Finally, the majority of the studies examining the correlates of sleep variability relied on retrospective, self-reported sleep data and neglected to include objective measures of nocturnal movement or activity. The latter point is important, as past studies have shown that intra-individual variability exists not only in sleep duration, but also in sleep efficiency and mobility (Knutson et al., 2007; van Hilten et al., 1993). Using both subjective and objective nightly measures of sleep will lead to a more precise and comprehensive understanding of the relationship between sleep patterns and psychological functioning. In the proposed study average sleep duration and fragmentation, and variability in these dimensions, are examined for their relation to negative affect in everyday life. Such knowledge holds important psychological health implications for a society in which sleep deprivation is becoming more common. First paragraph.

2.5 SLEEP AND PHYSICAL HEALTH

Dimensions of sleep have been implicated not only in psychological well-being, but also in physical health and disease. The following sections will review the literature linking sleep duration and fragmentation to health outcomes, with a focus on SAM activity as a mediating pathway linking sleep to disease. The limited data regarding variability in sleep-wake schedules and SAM functioning will then be addressed.

2.5.1 Sleep Duration and Health.

Sleep durations less than five or six hours a night have been linked to a variety of negative health outcomes (e.g., Amagai et al., 2004; Kojima et al., 2000; Mallon, Broman, & Hetta, 2005; Steptoe, Peacey, & Wardle, 2006). In particular, the relationship between relatively short sleep and cardiovascular outcomes has received increasing attention. In 2003, Ayas et al. reported that women who slept less than eight hours per night at baseline were more likely to experience a coronary event over the next ten years than those who typically slept eight hours. An average sleep duration of five or less hours per night is associated with atherosclerosis (Wolff, Volzke, Schwahn, Robinson, Kessler, & John, 2007) and increased risk for hypertension (Gangwisch et al., 2006). PSG-measured sleep fragmentation and sleep efficiency have also been related to cardiovascular risk markers, such as prothrombotic factors (von Kanel et al., 2007).

2.5.2 Sleep Duration and SAM Activity.

In an attempt to better understand the pathways linking sleep to cardiovascular disease, several studies have concentrated on the role of sleep in the homeostatic regulation of the sympathetic nervous system. The catecholamines epinephrine and norepinephrine are secreted by the adrenal medulla and the sympathetic nerve fibers in times of stress or arousal and are considered partial indicators of sympathetic activity (Henry, 1992). Prolonged elevation of catecholamine levels have been linked to cardiovascular outcomes, such as atherosclerosis, hypertension, and adverse clinical events after myocardial infarction (Kotlaba et al., 2005; Hauss, Bauch, Schulte, 1990; Mancia, Grassi, Giannattasio, & Seravalle, 1999). During sleep, sympathetic tone and

circulating levels of epinephrine and norepinephrine are reduced (Dodt et al., 1997; Irwin et al., 1999).

The nocturnal decline in catecholamine excretion may be due to several factors, including postural changes and an endogenous rhythm (the latter appears to be more relevant to epinephrine; Akerstedt, 1979), but there is also evidence to suggest that the act of sleep itself plays a role in catecholamine levels. A number of early experiments demonstrated that when other conditions were held constant, sleep deprivation reduced the nighttime trough normally observed in catecholamine levels (Akerstedt, 1979; Froberg, Karlsson, Levi, & Lidberg, 1972), and Steinberg, Guggenhelm, Bier and Snyder (1969) reported that one night of in-bed total sleep deprivation led to higher urinary levels of epinephrine and norepinephrine as compared to normal sleeping levels. Interpretation of these earlier studies is limited by a number of factors, including small sample sizes and questions regarding statistical design; however, a more recent study observed increases in circulating plasma levels of norepinephrine during one night of partial sleep deprivation (average sleep of 3.8 hours; Irwin et al., 1999), implicating sleep in the regulation of nocturnal SAM activity. The degree to which these associations persist outside of experimental paradigms is questionable, as no studies to date have reported a relationship between average sleep duration and catecholamines.

2.5.3 Sleep Fragmentation and SAM Activity.

In addition to sleep deprivation, sleep fragmentation has been linked to increased catecholamine levels. Poor PSG-measured sleep continuity is related to higher levels of nocturnal plasma norepinephrine in both patients with insomnia and elderly caregivers of Alzheimer's patients (Irwin, Clark, Kennedy, Christian Gillin, & Ziegler, 2003; Mausbach et al., 2006). An

experiment which housed individuals in an isolated environment for seven days found that actigraphy measures of sleep motor activity were related to heightened nocturnal norepinephrine excretion (Kraft et al., 2002). Finally, modest associations between self-reported awakenings after sleep onset and nighttime levels of norepinephrine have been reported in individuals living near the Three Mile Island nuclear generating station (Davidson, Fleming, & Baum, 1987). Therefore, increased nocturnal norepinephrine, in particular, may represent one pathway by which poor sleep is associated with cardiovascular endpoints. However, it is unclear whether such a relationship exists in individuals who are free from sleep disorders or heightened stress.

2.5.4 Sleep Variability and Health.

As described earlier, sleep duration and fragmentation are associated with an increased risk for several health problems. Few studies have focused on whether nightly changes in sleep patterns are associated with disease. Those that have done so have observed negative health outcomes among individuals whose sleep patterns are modified in the extreme; namely, shift workers. Rotating or alternating shift work, in which shifts are continuously rotated or changed according to a schedule, seems to pose a particularly high risk for obesity and type 2 diabetes (DiLorenzo et al., 2003; Sookoian et al., 2007; Suwazono et al., 2006). Moreover, several studies have reported increased rates of mortality due to ischaemic heart disease among rotating shift workers (Fujino, et al., 2006; Kawachi et al., 1995; Tuchsen, 1993). It has been hypothesized that the association between shift work and health outcomes is partly due to a desynchronization of the sleep-wake schedule and circadian biological rhythms. Although evidence is not conclusive, rotating shift work may offer less of a chance for the circadian adjustment of physiological systems as compared to fixed-night work, leading to an increased risk for disease (Bøggild & Knutsson,

1999; Totterdell, 2005). For example, rotating shift work is associated with increased biomarkers of CVD, such as inflammatory markers and the cluster of factors that make up the metabolic syndrome (Sookoian et al., 2007).

2.5.5 Sleep Variability and SAM Activity.

Few studies have addressed whether sleep patterns are associated with catecholamine levels. One intervention in policemen adjusted shift work schedules to be more in line with the naturally occurring circadian rhythm (Orth-Gomer, 1983). This modified sleep schedule resulted in initial increases in nocturnal urinary levels of epinephrine and norepinephrine, an increase which the author posited may have been due to the novelty of the new sleep-wake pattern. After three weeks of the new pattern, nighttime catecholamine levels in the intervention group fell significantly lower than those in the control condition. Fluctuations in diurnal catecholamine levels have also been observed during and after the night-shift portion of rotating shift schedules (Theorell & Akerstedt 1976; Vokac, Magnus, Jebens, & Gundersen, 1981).

It is unknown if less extreme nightly variability in sleep is also associated with altered catecholamine levels. Given that irregular sleep-wake schedules may contribute to nocturnal disturbances in insomnia (Kupfer & Reynolds, 1997; Summers et al., 2002), one possible mechanism linking variable sleep to urinary catecholamines is decreased sleep efficiency. In addition, the nighttime decline in SAM activity may not be as efficient or as pronounced in individuals who vary the timing and/or duration of their sleep on a nightly basis, as compared to those who keep regular sleep schedules. An alternative possibility is that heightened SAM activity during evening hours contributes to unstable sleep habits. For instance, chronic sympathetic hyperactivity has been suggested to play a role in sleep disturbances experienced by

those with insomnia and it is possible that similar dysregulation of the SAM axis may influence the timing or continuity of individuals' sleep on a more variable basis (Irwin et al., 1999). Therefore, while it is theoretically plausible that instability in sleep patterns is associated with elevations in the SAM axis, this relationship has not yet been investigated.

2.6 SUMMARY AND LIMITATIONS: SLEEP & SAM ACTIVITY

Sleep duration and fragmentation have been implicated in several diseases, including cardiovascular disease. Heightened nocturnal SAM activity, as indexed by catecholamine levels, has been hypothesized to be one potential mechanism linking sleep with cardiovascular morbidity. Although experimental sleep deprivation supports the role of sleep in sympathetic regulation, no studies have reported an association between short sleep duration and catecholamine levels. Furthermore, objective and self-report measures of sleep fragmentation are associated with increased norepinephrine among patients with insomnia or individuals dealing with chronic stress, but it is unknown if these associations are present in other samples.

Even less research has focused on the associations between the stability of sleep and health outcomes. Shift workers whose sleep and wake schedules are continuously changing have an increased risk for a variety of health problems. Although there are numerous potential pathways linking variable sleep and work schedules to increased morbidity, dysregulation of the SAM axis is one candidate mechanism. It is unknown whether more normative variability in sleep (as opposed to rotating shift work) is associated with increased nocturnal catecholamine production, as no studies have examined the relationship between sleep patterns and epinephrine and norepinephrine levels.

2.7 SLEEP, AFFECT, AND SAM ACTIVITY

Thus far, the associations between sleep and affect and sleep and SAM activity have been reviewed separately, but there is evidence to suggest that these three factors may be inter-related. As previously described, sleep duration, fragmentation, and perhaps variability, are associated with increased catecholamine levels. However, few, if any, of the studies reviewed above have considered measures of negative affect when assessing relationships between sleep and nocturnal SAM activity. This may be an important omission, as research shows that depression, anxiety, and hostility are related to increased levels of epinephrine and norepinephrine in both clinical and non-clinical samples (Janicki-Deverts et al., 2007; Musselman, Evans, & Nemeroff, 1998; Nesse, Cameron, Buda, McCann, Curtis, & Huber-Smith, 1985; Sherwood, Hughes, Kuhn, & Hinderliter, 2004). Therefore, sleep and negative affect may each be independently associated with nocturnal SAM activity, or they may have a synergistic effect, in which individuals who are both high in negative affect and have poor sleep habits exhibit the largest elevations in catecholamine levels. Consistent with the hypothesis that the interaction between sleep and affect influences nocturnal SAM activity is the fact that the majority of studies reporting associations between fragmented sleep and increased norepinephrine were conducted in individuals under chronic stress.

3.0 STATEMENT OF PURPOSE

The majority of sleep research in adults has emphasized inter-individual, as opposed to intra-individual differences, in dimensions of sleep. The first objective of this study is to learn more about nightly variability in a number of sleep parameters. Specifically, variability in the duration and fragmentation of sleep is examined within a sample of Black and White adults, and a number of demographic and lifestyle factors are tested for their correlations with nightly variability in sleep. Additionally, while a number of studies have linked short or variable sleep to mood, it remains unclear whether or not such associations exist in non-clinical adult samples or outside of experimental paradigms. Therefore, another objective of the current study is to examine the cross-sectional relationships between both average sleep and intra-individual variability in sleep and negative affect in a relatively healthy sample of adults. As past research has suggested that short, fragmented, or disrupted sleep patterns may also be associated with heightened nocturnal activity of the SAM system, the final purpose of this study is to investigate the relationships between these dimensions of sleep and nocturnal catecholamine levels. The moderating role of negative affect on the associations between sleep and SAM activity is also examined.

4.0 HYPOTHESES

The first set of hypotheses focuses on quantifying inter- and intra-individual variability in sleep parameters and determining the correlates of variability within individuals:

H1a. The amount of intra-individual variability in sleep parameters will equal or exceed the amount of inter-individual variability in sleep parameters.

The first objective of the proposed study is to characterize the stability of sleep patterns in a sample of Black and White adults over nine nights. Intra-individual variability in the duration and fragmentation of sleep will be quantified, and supplementary analyses will quantify intra-individual variability in the timing of sleep onset and ratings of sleep quality. It is hypothesized that substantial intra-individual variability in these factors exist, such that the amount of intra-individual variability is equal to or greater than the amount of inter-individual variability. Based on past research, it is hypothesized that both Blacks and women will have increased nightly variability in sleep compared to Whites and men (e.g., Knuston et al., 2007; vanHilten et al., 1993).

H1b. Intra-individual variability in sleep duration and fragmentation will be higher in individuals who report poorer global sleep quality, more stressful life events, and more health-damaging behaviors.

A number of factors will be investigated as correlates of sleep variability, including global sleep quality, sleep duration, stressful life events, and health behaviors. Based on past

findings (e.g., Brown et al., 2002; Medeiros et al., 2001), it is hypothesized that increased variability in sleep will be associated with poorer self-reported global sleep quality. Stressful life events, health-damaging behaviors (alcohol and nicotine use), and obesity all have been associated with sleep disruptions (Sadeh, Keinan, & Daon, 2004; Foster & Peters, 1999; Zhang, et al., 2006); therefore, it is hypothesized that each of these factors will be positively correlated with variability in sleep. Finally, as no studies have addressed the theoretically relevant question of how average sleep duration correlates with sleep variability, exploratory analyses will examine this relationship.

H1c. Nightly deviations from an individual's overall mean sleep duration will be a stronger predictor of the next morning ratings of sleep quality than actual sleep duration itself.

There may be individual differences in optimal sleep durations. Therefore, it is predicted that the nightly deviation from an individual's "typical" sleep duration is a better predictor of morning ratings of sleep quality than the absolute value of sleep duration itself.

The second set of hypotheses tests average sleep and intra-individual variability in sleep for their associations with negative affect and SAM activity:

H2a: A shorter average sleep duration and increased intra-individual variability in sleep duration each will be associated with increased negative affect.

H2b: Average sleep fragmentation and intra-individual variability in sleep fragmentation each will be positively associated with negative affect.

It is hypothesized that a shorter average sleep duration and increased intra-individual variability in duration each will be uniquely associated with increased negative affect, as characterized by depression, anxiety, and hostility levels. Similarly, it is hypothesized that an

increased fragmentation index and increased intra-individual variability in the fragmentation index each will be uniquely associated with increased negative affect.

H3a: A shorter average sleep duration and increased intra-individual variability in sleep duration each will be associated with increased nocturnal SAM activity.

H3b: Average sleep fragmentation and intra-individual variability in sleep fragmentation each will be positively associated with nocturnal SAM activity.

It is hypothesized that a shorter average sleep duration and increased intra-individual variability in duration each will be uniquely associated with higher nocturnal levels of epinephrine and norepinephrine. Similarly, it is hypothesized that an increased average fragmentation index and increased intra-individual variability in the fragmentation index each will be uniquely associated with higher nocturnal levels of epinephrine and norepinephrine.

H4: The associations between sleep (average duration, average fragmentation, or variability in these factors) and catecholamine levels will be stronger among those high in negative affect than those low in negative affect.

The proposed study allows for the exploration of models in which the interaction of sleep parameters and affect is associated with nocturnal catecholamine levels. Fragmented sleep and norepinephrine have been associated in samples under high stress or with insomnia; therefore, it is hypothesized that the associations between sleep (average duration, average fragmentation, or variability in these factors) and catecholamine levels are stronger among those high in negative affect than those low in negative affect (figure 1).

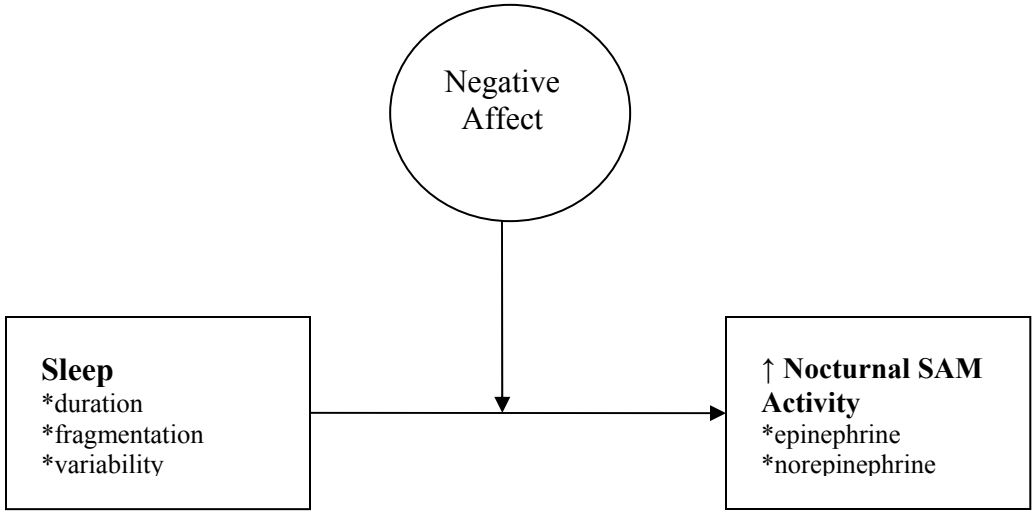


Figure 1. Hypothesized Moderating Role of Negative Affect on Associations between Sleep and SAM Activity

5.0 METHOD

5.1 RESEARCH PARTICIPANTS

Participants for the proposed study were originally recruited from the Heart Strategies Concentrating On Risk Evaluation (Heart SCORE) study, which is a single center, prospective, community-based participatory research cohort study investigating mechanisms for racial disparities in cardiovascular risk and attempting to decrease these disparities via a community-based intervention. Baseline enrollment in Heart SCORE began on June 16, 2003 and was completed on October 11, 2006. Eligibility criteria included age 45 to 75 years, residence in the greater Pittsburgh metropolitan area, ability to undergo baseline and annual follow-up visits, and absence of known co-morbidities expected to limit life expectancy to less than five years. Within this full cohort, the mean age at study entry was 59.1$\pm$7.5 years; 65% were female, 54% were white, 43% were black, 3% were of other race; 61% were married; and 81% had at least some college education beyond a high school diploma. The Institutional Review Board at the University of Pittsburgh approved the study protocol and all study participants provided written informed consent. Data collection included demographics, medical history, anthropometrics, lipids/lipoproteins, physical activity, and psychological status as previously described (Aiyer et al., 2007).

An ancillary sleep study, entitled Sleep SCORE, enrolled approximately equal ratios of male to female and Black to White participants from the Heart SCORE study sample. Exclusionary criteria for the sleep study included pregnancy; use of continuous positive airway pressure treatment for sleep-disordered breathing; medication for sleep problems on a regular basis; nighttime work schedule; medication for diabetes; and prior diagnosis of stroke, myocardial infarction, or interventional cardiology procedures. The reported analyses were based on the first 186 participants who completed the study out of the target of 225 participants.

5.2 PROCEDURE

Participants were recruited during Heart SCORE assessment visits. Study personnel approached potential participants and if interested and eligible, provided them with detailed information while obtaining written informed consent approved by the University of Pittsburgh Institutional Review Board. Participants were scheduled for the sleep study within three months of obtaining consent. The study protocol lasted 10 days. Two methods were used to collect the sleep data relevant to the current proposal. Actigraphs, which are watch-like activity monitors worn on the wrist to track rest and activity patterns via physical movement, were worn on Nights 1-9 to provide behavioral data regarding sleep duration and nighttime mobility. Diary reports were used in conjunction with actigraphy to track sleep and wake times, as well as subjective perceptions of sleep on nights and mornings 1-10 of the study. Overnight levels of urinary catecholamines were collected over 15-hour periods on Nights 2 and 4 of the study. Finally, in-home PSG sleep studies were conducted on Nights 1 and 2 and 24-hour ambulatory blood pressure monitoring was conducted on Nights 3 and 4 of the study. Although PSG and blood

pressure data are not relevant to the current study, it is possible that equipment or measurement processes may have increased variability in sleep, and therefore several analyses were adjusted for these variables.

5.3 MEASURES

5.3.1 Actigraphy.

An Actiwatch-64 (Respironics, Inc.) was worn on the non-dominant wrist continuously for 10 days to measure sleep duration (in conjunction with diary reports) and to assess fragmentation during sleep. Data were stored in 1-minute epochs and validated MINIMITTER software algorithms were used to estimate sleep parameters. Sleep start times and sleep end times were based upon actigraph-derived estimates of sleep onset and awakening, determined by movement. Assumed sleep duration is the amount of time between the actigraph-estimated sleep start and end times and does not account for awakenings throughout the night. The mean and standard deviation (SD) in assumed sleep duration over nine nights were calculated for each individual, representing average sleep duration and variability in sleep duration, respectively. The fragmentation index is a measure of nocturnal movement and was calculated as follows: ([%1-minute intervals of movement during sleep + % 1-minute intervals of immobility] divided by total 1-minute immobility intervals). The mean and the SD in the fragmentation index over nine nights were calculated for each individual, representing average activity and variability in activity, respectively.

5.3.2 Sleep Diary.

A 10-day diary was used for recording sleep times and perceptions of sleep quality. Each morning, participants recorded the time that they tried to go to bed on the preceding night and the time that they awoke in the morning. They also recorded how rested they felt upon awakening (0 = not at all – 5 = extremely) and the quality of the previous night's sleep (0 = very poor – 5 = average). Ratings of feeling rested and sleep quality were standardized and averaged to create a composite variable representing overall sleep quality. Means and SDs for time of sleep onset and ratings of sleep quality were calculated for each participant.

5.3.3 Negative Affect.

The Center for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977), the Spielberger Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, & Lushene, 1970), and the Cook-Medley Hostility Scale (Ho; Cook & Medley, 1954) were used to measure symptoms of depression, anxiety, and hostility, respectively. The sleep item was excluded from the total CES-D score. Given that CES-D, STAI, and Ho scores were significantly correlated with one another (rs = .31 - .36, ps < .001) and the theoretical overlap that may exist among these three affective dispositions (Suls & Bunde, 2005), scores from the CES-D, STAI, and Ho were standardized and then averaged to create a composite variable indicating negative affect.

5.3.4 Urinary Catecholamines.

Catecholamines were obtained from overnight urine collections that took place on Nights 2 and 4 of the study. Participants were asked to void their bladders normally at 6 p.m. and to collect all urine voided thereafter until 9:00 a.m. the following morning. Participants recorded the time period over which they collected their urine in a written log. Containers included the preservative sodium metabisulfite, and they were kept on ice until samples were aliquotted and frozen in the laboratory. Catecholamine levels were determined by high performance liquid chromatography with electrochemical detection and corrected for urine volume. Sensitivity was .33 ng/ml for epinephrine and 1.33 ng/ml for norepinephrine. The between-assay variation ranged from 10.1-13.2% for epinephrine and 8.5-14.0% for norepinephrine. None of the participants had elevated creatinine > 1.5 mg/dl. Mean epinephrine and norepinephrine levels were calculated by averaging the values obtained on Nights 2 and 4.

5.3.5 Potential Correlates of Sleep Variability.

A number of measures were hypothesized to be associated with sleep variability, including global sleep quality, average sleep duration, stressful life events, health behaviors, and BMI. The Pittsburgh Sleep Quality Index (PSQI; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) measured *global sleep quality* over the previous month. Nineteen individual items on the PSQI are grouped to create seven component scores (e.g., subjective sleep quality, sleep latency, sleep duration, etc.). These subscores are summed to generate a global score between 0 and 21, with higher scores indicating worse sleep quality. *Average sleep duration* was based on actigraphy sleep duration values averaged across the nine nights, as previously described. *Stressful life*

events were assessed using two measures. The first assessed the number of chronic problems that had been ongoing for at least 12 months and were described as still being "very stressful," and the second assessed the number of stressful events that had occurred in the past six months and were described as still being "very upsetting." Total numbers of items endorsed on each scale were standardized and then averaged to create a composite stressful life events score. *Health behaviors* assessed in the daily diary included self-reported alcohol and nicotine use. Average number of alcoholic beverages consumed over the study period and smoking status (yes/no) were used in analyses. *BMI* was calculated by dividing weight (in kilograms) by height squared (in meters).

Exploratory analyses tested for differences in sleep variability by Framingham Risk group and cardiac/BP medication use. *Framingham Risk group* was determined at HeartSCORE baseline visits. The Framingham Risk Index estimates risk of heart attack in the next 10 years, based on sex, age, smoking status, blood pressure, total cholesterol, and presence of diabetes mellitus. Based on this index, participants were classified as being at either low-risk or moderate/high-risk. Reports of typical *medication use* were collected during the time of the sleep study.

5.4 ANALYTIC PLAN

Hypotheses were tested statistically in the following manner:

H1 (a). The amount of intra-individual variability in sleep parameters will equal or exceed the amount of inter-individual variability.

Multi-level modeling was used to determine the proportion of total variance attributable to within-individual differences (at Level 1) and between-individual differences (at Level 2) in sleep parameters. Main analyses examined the variability in assumed sleep duration and fragmentation, and supplementary analyses examined the variability in time of sleep onset and ratings of sleep quality. A dummy variable (weeknight yes/no) was included in the Level 1 equation to adjust for night of the week effects when examining within- and between-individual variance components. The intraclass correlation coefficient (ICC), a statistic for quantifying the relative magnitude of within and between-person variance components in a multi-level model, was calculated for sleep parameters by dividing the between-person variance by the total variance in these two parameters. Analysis of variance was used to examine differences in intra-individual variability in sleep duration, fragmentation, bedtime, and sleep quality by sex and race groups.

H1 (b). Intra-individual variability in sleep duration and fragmentation will be higher in individuals who report poorer global sleep quality, more stressful life events, and more health-damaging behaviors.

A series of Pearson correlations tested if intra-individual variability values in sleep duration and fragmentation (as measured the SDs) were higher among individuals with

poorer global sleep quality, shorter average sleep duration, more stressful life events, more alcohol and nicotine use, and higher BMIs. To assess the unique associations between intra-individual variability in sleep and the above factors, a series of multiple linear regression analyses were conducted, adjusting for average duration and fragmentation, as appropriate.

H1 (c). Nightly deviations from an individual's overall mean sleep duration will be a stronger predictor of morning ratings of sleep quality than sleep duration itself.

Multi-level models were used to determine whether nightly deviations from an individual's typical sleep duration were more strongly associated with morning ratings of sleep quality than nightly values of sleep durations. For each participant, nine nightly "deviation scores" were calculated, representing the difference between sleep on an individual night and the participant's mean sleep duration (averaged across nine nights). After controlling for night of the week, nightly sleep duration and nightly deviation scores were used to predict morning ratings of sleep quality at Level 1 of the model. An identical model was adjusted for PSG and BP measurement effects. The β values representing the effects of sleep deviation and sleep duration were compared to determine the strength of the associations between these two variables and morning ratings of sleep quality. Race and sex variables were included in the Level 2 equation to model differences by race and sex in the effects of sleep deviation and duration on sleep quality.

A series of multiple linear regression models were used to test the associations among sleep parameters, negative affect, and SAM activity in hypotheses 2-4. Covariates for these models included demographic variables (age, sex, race) and physical health variables (BMI,

Framingham risk group [high/moderate vs. low], medication use [cardiac medication/BP medication use), as these variables may be associated with negative affect and/or SAM activity.

H2 (a): A shorter average sleep duration and increased intra-individual variability in sleep duration each will be associated uniquely with increased negative affect.

Linear regression was used to determine whether or not average self-reported sleep duration and intra-individual variability in assumed sleep duration were associated with increased negative affect (the composite score of depression, anxiety, and hostility). Composite negative affect was considered as the dependent variable. Covariates were entered in the first step of the model, the SD for intra-individual variability in the second step, and mean sleep duration in the final step. Exploratory analyses tested for sex and race differences in these associations.

H2 (b): Actigraphy-measured average sleep fragmentation and intra-individual variability in sleep fragmentation will be positively and uniquely associated with negative affect.

Linear regression was used to determine whether or not average sleep fragmentation and intra-individual variability in sleep fragmentation were associated with increased negative affect, using an identical process to the one described above.

H3 (a): A shorter average sleep duration and increased intra-individual variability in sleep duration each will be associated uniquely with increased nocturnal SAM activity.

Linear regression was used to determine if average self-reported sleep duration and intra-individual variability in assumed sleep duration were associated with increased nocturnal SAM activity. Average levels of epinephrine from Nights 2 and 4 and average levels

of norepinephrine from Nights 2 and 4 were considered as the dependent variables. Covariates were entered in the first step of the model, the SD for intra-individual variability in duration in the second step, and mean sleep duration in the final step. Exploratory analyses tested for sex and race differences in these associations.

H3 (b): Actigraphy-measured average sleep fragmentation and intra-individual variability in sleep fragmentation will be positively and uniquely associated with nocturnal SAM activity.

Linear regression models were used to determine if average sleep fragmentation and intra-individual variability in sleep fragmentation were associated with increased nocturnal SAM activity, using an identical process to the one described above.

H4: The associations between sleep (average duration, average fragmentation, or variability in these factors) and catecholamine levels will be stronger among those high in negative affect than those low in negative affect.

A series of four multiple linear regression models examined whether the associations between sleep parameters and nocturnal SAM activity were stronger among those high in negative affect versus those low in negative affect. The interaction between composite negative affect and each of the four sleep parameters (average duration, variability in duration, average fragmentation, variability in fragmentation) was entered in separate regression models, after inclusion of the main effects and covariates in the first step.

6.0 RESULTS

6.1 SAMPLE CHARACTERISTICS

One participant had missing actigraphy data and one participant had missing sleep fragmentation data only. Two participants reported bed time values that differed from actigraphy estimates by more than two hours and were determined to be outliers (a total of ten data points between two participants). As the intra-individual variability in these participants' sleep parameters could not be calculated due to the reduced number of available data points, these two participants were dropped from analyses. Therefore, analyses involving sleep duration and sleep fragmentation were based on final sample sizes of 184 and 183 participants, respectively.

Table 1 displays descriptive information regarding demographics, psychosocial factors, and catecholamine levels for the entire sample. Slightly more than half of the participants were men, 75 were Black, 105 were non-Hispanic White, and four were Asian (White and Asian participants were combined into one group for analytical purposes). Mean age was 59.6 years and mean BMI was 29.5. About half of the participants were classified as being at medium-to-high risk for a cardiovascular event based on Framingham risk criteria, and 50 were taking one of four cardiac medications that were found to be associated with sleep and/or catecholamines in this sample (angiotensin-II receptor blockers, angiotensin-converting enzyme inhibitors, alpha-1 blockers, and alpha-2 agonists). Because epinephrine and norepinephrine data were positively

skewed, they were log-transformed for analyses; the non-transformed values are displayed in the table.

Table 1. Sample Characteristics

Variable	*n (%)*	*M (SD)*	*Range*
Men	97 (52.7)		
Race			
White	105 (57.1)		
Black	75 (40.8)		
Asian	4 (2.1)		
Medium/High Framingham Risk Group	92 (50.0)		
Cardiac/Hypertensive Medication Use	50 (27.2)		
Age		59.6	46 - 78
Body Mass Index		29.5 (5.0)	17.9 – 45.3
Epinephrine ng/ml		3.9 (2.8)	.6 – 17.8
Norepinephrine ng/ml		35.0 (21.8)	4.3 – 110.3
CES-D Score		9.7 (9.4)	0 – 37
STAI Score		6.0 (5.0)	0 – 21
Ho Score		8.5 (4.2)	1.0 – 19
Pittsburgh Sleep Quality Index		6.3 (3.4)	0 - 16
Stressful Life Events		.56 (.8)	0 – 4
No. of Alcoholic Drinks (over study)		4.8 (8.3)	0 - 39
Physical Activity Rating		7.9 (6.6)	0 - 24
Current Smokers	19 (10.3)		

6.2 SLEEP PARAMETERS

Table 2 displays descriptive information regarding sleep parameters. Paired t-test comparisons showed no differences in intra-individual variability (as measured by the standard deviation of an individual's values over nine nights) in duration, fragmentation, or bedtime over the first four nights of the study compared to the final four nights (*p*s > .2); however, there was more intra-individual variability in diary ratings of sleep quality over the first four nights. In terms of means, participants slept for a significantly longer duration and had earlier bedtimes during Nights 1-4 versus Nights 6-9. There were no differences in mean fragmentation or mean diary ratings of sleep quality (*p*s > .3*)*.

Table 2. Means and Standard Deviations of Sleep Parameters Across the Study Period and by Nights 1-4 vs. Nights 6-9

	Nights 1-9		Nights 1-4	Nights 6-9
Variable	Mean (SD)	Range	Mean (SD)	Mean (SD)
Sleep Duration				
Mean (hrs)	6.7 (.9)	4.5 – 9.4	6.8 (.9)†	6.5 (1.1) †
Intra-Individual Variability (mins)	67.3 (28.7)	.3 – 3.6	63.7 (37.6)	62.3 (38.7)
Sleep Fragmentation				
Mean	32.6 (11.6)	12.4 – 75.6	32.6 (12.0)	32.6 (13.0)
Intra-Individual Variability	10.6 (4.9)	2.6 – 27.8	10.3 (5.8)	9.8 (5.7)
Bedtime				
Mean	23:29 (63.5)	20:39 – 3:24	23:22 (63.8) †	23:35 (70.2) †
Intra-Individual Variability (mins)	48.6 (25.6)	9.0 - 160	42.9 (27.1)	43.2 (32.1)
Diary Sleep Quality				
Mean	2.3 (.5)	.4 – 3.5	2.3 (.6)	2.3 (.6)
Intra-Individual Variability	.7 (.2)	0 – 1.5	.6 (.3) †	.5 (.3) †

† Nights 1-4 significantly different from Nights 6-9 at $p < .001$.

6.2.1 Sleep Variability by Sex and Race.

Table 3 displays the unadjusted mean values for intra-individual variability in sleep duration, fragmentation, bedtime, and sleep quality by sex and race groups. Also shown are the significance values from analysis of variance tests comparing sex and race groups after controlling for age, race (when appropriate), sex (when appropriate), BMI, Framingham risk group, medication use, and the relevant mean sleep parameter (i.e., analyses using intra-individual variability in sleep duration as the outcome variable were adjusted for mean sleep duration). Women had more intra-individual variability in sleep duration and marginally more intra-individual variability in bedtimes and diary ratings of sleep quality than men. Blacks had more intra-individual variability in sleep fragmentation and bedtimes than Whites.

Table 3. Unadjusted Means (SDs) in Intra-Individual Variability in Sleep Parameters by Sex and Race

	Sex			Race		
Variable	Men (*n = 97*)	Women (*n = 87*)	*p*	White (*n = 109*)	Black (*n = 75*)	*p*
SD Sleep Duration (mins)	63.0 (27.6)	72.0 (29.2)	.01	63.0 (28.9)	73.4 (27.3)	.22
SD Sleep Fragmentation	10.1 (4.3)	11.0 (5.3)	.20	9.3 (4.5)	12.4 (4.9)	.006
SD Bedtime	44.4 (22.6)	53.3 (28.0)	.09	41.3 (19.9)	59.3 (29.2)	< .001
SD Diary Sleep Quality	.6 (.2)	.7 (.3)	.09	.7 (.3)	.7 (.2)	.62

Note: Intra-individual variability in the above variables were measured using standard deviations across nine nights. Mean values displayed in cells are unadjusted, while *p* values are from analysis of variance tests adjusted for age, sex, race, BMI, Framingham risk group, medication use, and the relevant mean sleep parameter.

6.2.2 Sleep Variability by Framingham Risk Group and Medication Use.

Analysis of variance tests showed that individuals in the moderate/high Framingham risk group had marginally more variability in sleep duration ($F = 3.3$, $p = .07$) after controlling for age, race, sex, BMI, and mean sleep duration than those in the low Framingham risk group. There were no differences between the high and low Framingham risk groups in terms of variability in fragmentation ($F = .61$, $p = .4$). Individuals who were taking angiotensin-II receptor blockers, angiotensin-converting enzyme inhibitors, alpha-1 blockers, or alpha-2 agonists did not differ in variability in sleep duration ($F = .20$, $p = .6$), nor in variability in fragmentation ($F = 2.2$, $p = .1$), compared to those who were not taking these medications.

6.3 HYPOTHESIS 1

6.3.1 1a. Within- vs. Between-Individual Differences in Actigraphy Sleep Parameters.

Using multi-level modeling, the total variance in sleep duration attributable to within-individual differences and between-individual differences after controlling for number of weekday nights versus weekend nights was calculated. An intercept-only model showed that the estimated between-person variance was .632 and the estimated within-person variance was 1.528. The intra-class correlation coefficient (ICC), which indicates the proportion of total variability attributable to between-individual differences, was calculated as .30 (conversely, 70% of the

variance in sleep duration was attributable to variability within individuals). Repeating the same procedure for sleep fragmentation showed that the variance between individuals in fragmentation indices after controlling for number of weekdays versus weekends was 118.082 and the variance within individuals was 134.936. Therefore, the ICC for the fragmentation index was .45 (conversely, 55% of the variance in sleep fragmentation was attributable to variability within individuals). Repeating these analyses after controlling for the presence of PSG and BP measurement equipment did not change the reported results.

ICCs were also calculated for bedtimes and morning ratings of sleep quality. The ICC for bedtimes was .55 (slightly less than half of the variance was due to within-individual differences) and the ICC for diary ratings of sleep quality was .33 (nearly 70% of the variance was due to within-individual differences). Adjustment for the presence of PSG and BP measurement equipment did not change the reported ICCs.

6.3.2 1b. Intra-Individual Variability in Sleep and Psychosocial Factors.

Table 4 displays the bivariate correlations between variability in sleep duration and fragmentation (as measured by their SDs), mean sleep duration, mean sleep fragmentation, self-reported sleep quality on the PSQI, stressful life events, alcohol use, exercise, and BMI. Increased variability in sleep duration was associated with poorer sleep quality on the PSQI and more stressful life events, and was marginally associated with a shorter average sleep duration, but was not related to exercise or alcohol use. Linear regression analyses were conducted to test the associations between intra-individual variability in sleep duration, PSQI scores, and stressful life events after adjustment for age, sex, race, BMI, Framingham risk group, and medication

status. Increased intra-individual variability in sleep was independently associated with more stressful life events (B = .005, p = .02) and higher PSQI scores (B = .02, p = .03), and these relationships persisted after controlling for mean sleep duration.

Increased variability in sleep fragmentation was correlated with a shorter average sleep duration, more stressful life events, and less alcohol use, and was marginally associated with poorer sleep quality on the PSQI. In regression analyses controlling for age, sex, race, BMI, Framingham risk group, and medication status, greater variability in sleep fragmentation was marginally associated with more stressful life events (B = .02, p =.07). The strength of this relationship increased after entering mean fragmentation values in the model (B = .03, p = .03). Greater variability in sleep fragmentation was also associated with less alcohol use (B = -.04, p = .01) in linear regression models. Analysis of variance tests determined that there were no differences in intra-individual variability in duration or fragmentation by smoking status (ps > .1).

Table 4. Bivariate Correlations between Intra-Individual Standard Deviations in Sleep Duration and Fragmentation and Covariates

Variable	1	2	3	4	5	6	7	8	9
1. SD Duration	—								
2. SD Fragmentation	.32**	—							
3. Mean Duration	-.14†	-.26**	—						
4. Mean Fragmentation	.08	.41**	-.04	—					
5. Pittsburgh Sleep Quality Index	.21**	.12	-.13†	.09	—				
6. Stressful Life Events	.23**	.16*	-.04	-.07	.10	—			
7. Mean No. Alcohol Drinks	-.08	-.20**	-.11	.04	-.11	-.01	—		
8. Physical Activity Rating	-.12	-.18*	.08	-.10	-.30**	-.16*	.06	—	
9. BMI	.05	.13†	-.17*	.04	.10	.11	-.18*	-.15*	—

† Correlation is significant at $p < .10$ level.
* Correlation is significant at $p \leq .05$ level.
** Correlation is significant at $p \leq .01$ level.

6.3.3 1c. Absolute Sleep Duration vs. Nightly Deviations from the Mean as Predictors of Sleep Quality.

Multi-level models were used to compare whether nightly deviations from an individual's typical sleep duration or nightly absolute values of sleep duration were more strongly associated with morning ratings of sleep quality. Results are shown in Table 5. Model A, which tested nightly sleep duration as a predictor of morning ratings of sleep quality after controlling for weeknight versus weekend night status, showed that increased lengths of sleep were associated with reports of better sleep quality the following morning. Model B included both nightly sleep duration and nightly deviations from an individual's mean sleep duration scores as predictors of morning reports of sleep quality after controlling for weeknight status. In this model, deviation scores were significant predictors of morning reports of sleep quality, while nightly durations of sleep fell to non-significance. When race and sex were added to the model as Level-2 variables (Model C), sex was associated with sleep quality, such that men reported better sleep quality than women. The final model (Model D) included all of the variables reported above, as well as a sex-by-deviation and a race-by-deviation interaction term in order to explore whether associations differed by sex and race, respectively. The sex-by-deviation score interaction term was associated with sleep quality, suggesting that deviations from mean sleep duration were more strongly related to sleep quality in men compared to women.

Table 5. Multi-Level Models Testing Nightly Sleep Duration and Deviations in Duration as Predictors of Morning Ratings of Sleep Quality

	Parameter	*Model A*	*Model B*	*Model C*	*Model D*
Fixed Effects	Intercept β_0	1.800** (.102)	2.542** (.287)	2.33** (.295)	2.33** (.295)
	Weekday β_1	-.053 (.038)	-.051 (.038)	-.051 (.038)	-.051 (.038)
	Duration β_2	.001** (.0002)	-.001 (.0007)	-.0002 (.0007)	-.0002 (.0007)
	Deviation β_3		.002** (.0007)	.002* (.0008)	.001† (.0008)
	Sex β_4			.206** (.076)	.206** (.076)
	Race β_5			-.047 (.081)	-.047 (.081)
	Sex-by-Deviation β_6				.001* (.0005)
	Race-by-Deviation β_7				-.0002 (.0005)
Variance Components	σ^2_{ε}	.425** (.016)	.425 ** (.016)	.425** (.016)	.423** (.016)
	$\sigma^2_{\upsilon 0}$	.226** (.029)	.216** (.028)	.206** (.026)	.206** (.026)

$^{\dagger} \leq .10$ * $\leq .05$ ** $\leq .01$

Model A -2 log L = 3576.1
Model B -2 log L = 3568.6
Model C -2 log L = 3561.5
Model C -2 log L = 3557.4

6.4 HYPOTHESIS 2

6.4.1 2a. Sleep Duration and Negative Affect.

The left side of Table 6 displays the regression coefficients and standard errors for linear regression analyses testing the associations between variability and mean sleep duration with negative affect (the composite of CES-D, STAI, and Ho scores). After controlling for age, sex, race, BMI, Framingham Risk group, and cardiac medication status, the association between intra-individual variability in sleep duration and negative affect was non-significant. Similarly, there was no association between mean sleep duration and negative affect. The interaction between sex and intra-individual variability in sleep duration was marginally significant (B = .006, p = .1). In exploratory analyses in which the sample was stratified by sex, increased intra-individual variability in sleep duration was associated with negative affect in men (B = .005, p = .05), but not in women (B =-.003, p = .4). The relationship between increased variability in sleep and negative affect in men fell to marginal significance after controlling for mean sleep duration (B =.005, p = .08). Interactions between sex and mean sleep duration and between race and sleep duration parameters were non-significant (ps > .1).

6.4.2 2b. Sleep Fragmentation and Negative Affect .

The right side of Table 6 displays the regression coefficients and corresponding standard errors for linear regression analyses testing the associations between variability and mean sleep fragmentation with negative affect. After controlling for age, sex, race, BMI, Framingham Risk group, and cardiac medication status, the association between intra-individual variability in sleep

fragmentation and negative affect was found to be non-significant. Similarly, there was no association between mean sleep fragmentation and negative affect. None of the race or sex by fragmentation interaction terms was significantly associated with negative affect. In exploratory analyses in which the sample was stratified by sex, increased intra-individual variability in sleep fragmentation was associated with negative affect in men (B =.03, p = .05), but not in women (B =.004, p = .9). The relationship between increased variability in fragmentation and negative affect in men fell to marginal significance after controlling for mean sleep fragmentation (B =.03, p = .07).

Table 6. Intra-Individual Variability and Average Sleep Parameters as Predictors of Negative Affect

Duration			Fragmentation		
Variable	*B (SE)*	ΔR^2	*Variable*	*B (SE)*	ΔR^2
Step 1			Step 1		
age	-.01 (.008)		age	-.01 (.008)	
sex	-.14 (.10)		sex	-.14 (.10)	
race	.08 (.11)		race	.07 (.11)	
BMI	-.003 (.01)		BMI	-.002 (.01)	
risk group	-.12 (.11)		risk group	-.13 (.11)	
cardiac drug	.11 (.12)		cardiac drug	.11 (.12)	
		.036 [a]			.037[a]
Step 2			Step 2		
SD duration	.001 (.002)	--	SD fragmentation	.01 (.01)	--
Step 3			Step 3		
Mean duration	-.001 (.001)	--	Mean fragmentation	-.001 (.005)	--

Note: Sex coded +1 for men and 0 for women; race coded +1 for White and 0 for Black; risk group coded +1 for Medium/High Framingham Risk and 0 for Low Framingham Risk; cardiac drug coded +1 for cardiac/hypertensive medication use and 0 for no cardiac/hypertensive medication use.

[a] the slight difference in R^2 values from the model testing duration and the model testing fragmentation is due to the loss of one participant in the fragmentation model.

6.5 HYPOTHESIS 3

6.5.1 3a. Sleep Duration and Epinephrine.

Table 7 displays the regression coefficients and corresponding standard errors for linear regression analyses testing the associations between variability and mean sleep duration with nocturnal epinephrine levels (averaged across two nights). Race and sex were associated with nocturnal epinephrine, such that both Blacks and men had higher levels of epinephrine than Whites and women, respectively. Cardiac medication use and higher BMIs were marginally associated with lower epinephrine levels. After controlling for age, sex, race, BMI, Framingham Risk group, and cardiac medication status, neither intra-individual variability in sleep duration nor mean sleep duration was significantly associated with epinephrine levels. Interactions between race and sleep duration parameters and between sex and sleep duration parameters were non-significant (*p*s > .10).

6.5.2 3a. Sleep Duration and Norepinephrine.

Table 7 also displays the regression coefficients and corresponding standard errors for linear regression analyses testing the associations between variability and mean sleep duration with nocturnal norepinephrine levels (averaged across two nights). Blacks and men were more likely to have higher levels of norepinephrine than Whites and women, respectively. After controlling for covariates, neither intra-individual variability in sleep duration nor mean sleep duration was

significantly associated with norepinephrine levels. Interactions between race and duration parameters and between sex and duration parameters were non-significant (*p*s > .10).

Table 7. Intra-Individual Variability in Sleep Duration and Mean Sleep Duration as Predictors of Nocturnal Catecholamine Levels

	Epinephrine			Norepinephrine	
Variable	*B (SE)*	ΔR^2	*Variable*	*B (SE)*	ΔR^2
Step 1			Step 1		
age	-.003 (.006)		age	-.004 (.007)	
sex	.32 (.08)**		sex	.21 (.10)*	
race	-.23 (.09)**		race	-.22 (.10)*	
BMI	-.02 (.009)†		BMI	.01 (.01)	
risk group	-.11 (.09)		risk group	.11 (.11)	
cardiac drug	-.18 (.10)†		cardiac drug	-.16 (.11)	
		.146**			.086*
Step 2			Step 2		
SD duration	.001 (.001)	--	SD duration	.001 (.002)	--
Step 3			Step 3		
Mean duration	.001 (.001)	--	Mean duration	-.001 (.001)	--

† ≤ .10 * ≤ .05 ** ≤ .01

Note: Sex coded +1 for men and 0 for women; race coded +1 for White and 0 for Black; risk group coded +1 for Medium/High Framingham Risk and 0 for Low Framingham Risk; cardiac drug coded +1 for cardiac/hypertensive medication use and 0 for no cardiac/hypertensive medication use.

6.5.3 3b. Sleep Fragmentation and Epinephrine.

Table 8 displays the regression coefficients and corresponding standard errors for linear regression analyses testing the associations between variability and mean sleep fragmentation with nocturnal epinephrine levels. After controlling for covariates, neither intra-individual variability in fragmentation nor mean fragmentation was significantly associated with epinephrine levels. Interactions between race and fragmentation parameters were non-significant, as was the sex-by-mean fragmentation interaction (*p*s > .10). The sex-by-variability in fragmentation interaction term was marginally significant (B = .03, p = .1). Stratification of the sample by sex showed that there was an association between intra-individual variability in fragmentation and epinephrine in men (B = .03, p = .05) but not in women (B = -.01, p = .4). This association was maintained after adjustment for mean fragmentation (B = .03, p = .04).

6.5.4 3b. Sleep Fragmentation and Norepinephrine.

Table 8 also displays the regression coefficients and corresponding standard errors for linear regression analyses testing the associations between variability and mean sleep fragmentation with nocturnal norepinephrine levels. After controlling for covariates, increased intra-individual variability in fragmentation was marginally associated with increased norepinephrine levels. This association reached significance after controlling for mean sleep fragmentation (B = .024, p = .03). A trend in which less mean fragmentation was associated with increased norepinephrine

was also observed. Interactions between race and fragmentation parameters and between sex and fragmentation parameters were non-significant (*p*s > .10).

Table 8. Intra-Individual Variability in Sleep Fragmentation and Mean Sleep Fragmentation as Predictors of Nocturnal Catecholamine Levels

	Epinephrine			Norepinephrine	
Variable	*B (SE)*	ΔR^2	*Variable*	*B (SE)*	ΔR^2
Step 1			Step 1		
age	-.002 (.006)		age	-.003 (.007)	
sex	.32 (.08)**		sex	.20 (.10)*	
race	-.24 (.09)**		race	-.23 (.10)*	
BMI	-.02 (.009)†		BMI	.01 (.01)	
risk group	-.13 (.09)		risk group	.10 (.11)	
cardiac drug	-.19 (.10)†		cardiac drug	-.17 (.11)	
		.149**			.088*
Step 2			Step 2		
SD fragmentation	.007 (.009)	--	SD fragmentation	.016 (.01) †	.01†
Step 3			Step 3		
Mean fragmentation	.001 (.004)	--	Mean fragmentation	-.009 (.005) †	.02*

† ≤ .10 * ≤ .05 ** ≤ .01. [a] the association between SD fragmentation and norepinephrine is significant at $p < .05$ in Step 3 of the model.

Note: Sex coded +1 for men and 0 for women; race coded +1 for White and 0 for Black; risk group coded +1 for Medium/High Framingham Risk and 0 for Low Framingham Risk; cardiac drug coded +1 for cardiac/hypertensive medication use and 0 for no cardiac/hypertensive medication use.

6.6 HYPOTHESIS 4

6.6.1 Sleep Duration-by-Negative Affect Interactions

6.6.1.1 Epinephrine.

The interactions between intra-individual variability in sleep duration and negative affect and between mean sleep duration and negative affect were tested for their associations with nocturnal epinephrine and norepinephrine levels in linear regression models. After controlling for covariates, the variability in duration by negative affect interaction was associated with epinephrine levels (B = .005, p = .05). Plotting the simple slopes at one SD above and below the mean of negative affect (e.g., Dearing & Hamilton, 2006) showed that increased variability in sleep duration was associated with increased epinephrine levels at high levels of negative affect (B = .003, p = .15), and there was an opposite relationship at low levels of negative affect (B = -.004, p = .15), although neither slope reached statistical significance (Figure 2). The interaction between mean sleep duration and negative affect was not associated with epinephrine levels (B = -.001, p = .22).

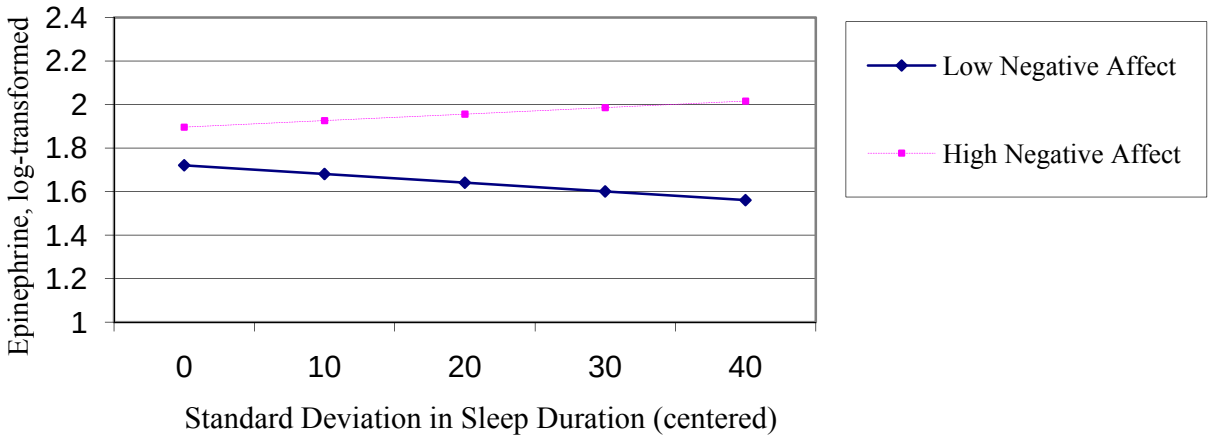


Figure 2. Simple Slopes of Epinephrine on Intra-Individual Variability in Sleep Duration at Low and High Levels of Negative Affect

6.6.1.2 Norepinephrine.

The variability in duration by negative affect interaction was marginally associated with norepinephrine levels (B = .005, p = .08). Plotting the simple slopes at one SD above and below the mean of negative affect showed that increased variability in sleep duration was associated with increased norepinephrine levels at high levels of negative affect (B = .003, p = .12) and there was an opposite relationship at low levels of negative affect (B = -.003, p = .3), although neither slope was statistically significant (Figure 3). Additionally, the interaction between mean sleep duration and negative affect was marginally associated with norepinephrine levels (B = -.003, p = .08). At one SD above the mean of negative affect, shorter sleep duration was marginally related to increased norepinephrine (B = -.002, p = .08), but there was no association

between duration and norepinephrine at low levels of negative affect (B = .001, p = .5) (Figure 4).

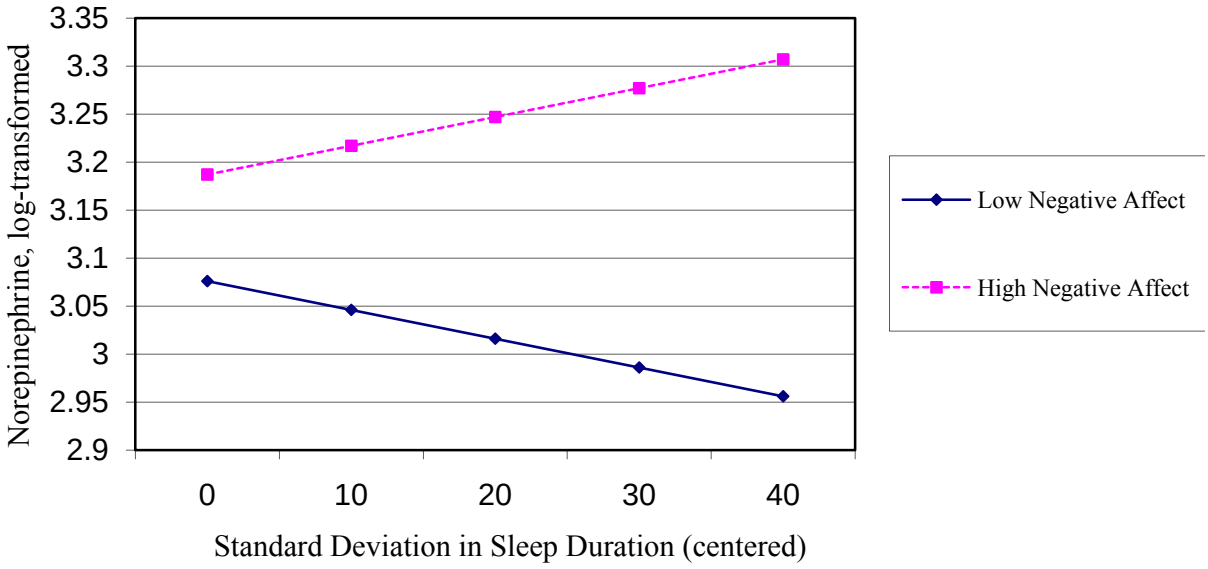


Figure 3. Simple Slopes of Norepinephrine on Intra-Individual Variability in Sleep Duration at Low and High Levels of Negative Affect

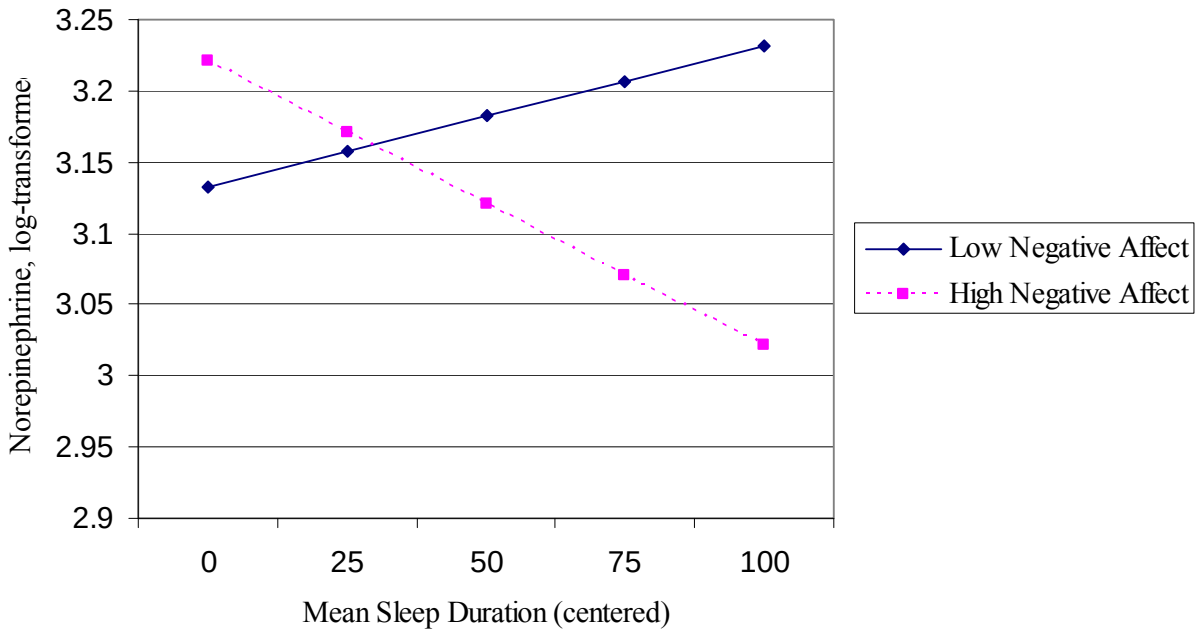


Figure 4. Simple Slopes of Norepinephrine on Mean Sleep Duration at Low and High Levels of Negative Affect

6.6.2 Sleep Fragmentation-by-Negative Affect Interactions

6.6.2.1 Epinephrine.

After controlling for covariates, the interaction between variability in sleep fragmentation and negative affect was associated with epinephrine levels (B = .02, p = .07). Increased intra-individual variability was marginally associated with increased epinephrine at one standard deviation above the mean of negative affect (B = .017, p = .1), but there was no association at one standard deviation below the mean of negative affect (B = -.011, p = .4) (Figure 5). The mean fragmentation by negative affect interaction was associated with epinephrine levels (B = .015, p = .008). Increased fragmentation was associated with increased epinephrine at one

standard deviation above the mean of negative affect (B = .011, p =.05), but there was an opposite relationship at one standard deviation below the mean of negative affect (B = -.01, p = .07) (Figure 6).

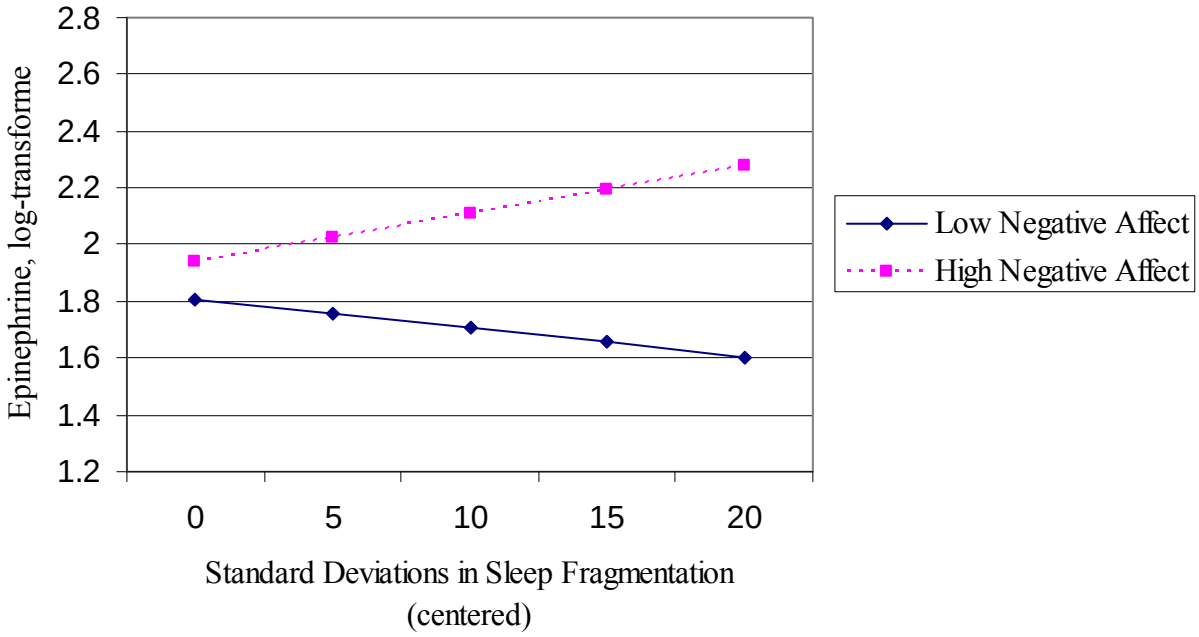


Figure 5. Simple Slopes of Epinephrine on Intra-Individual Variability in Sleep Fragmentation at Low and High Levels of Negative Affect

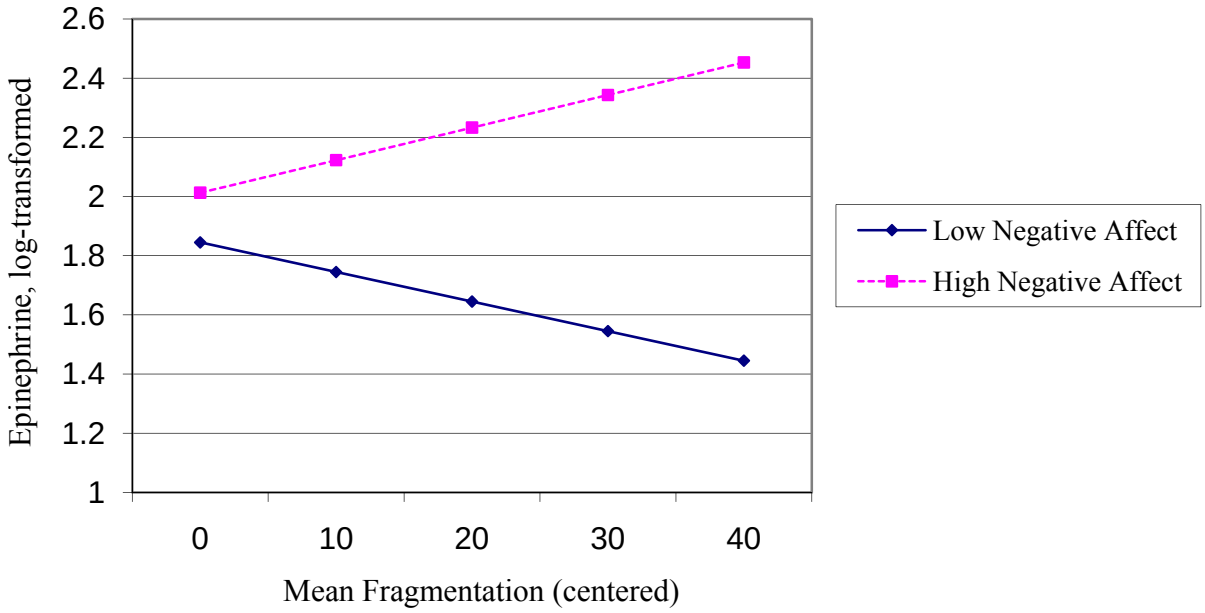


Figure 6. Simple Slopes of Epinephrine on Mean Sleep Fragmentation at Low and High Levels of Negative Affect

6.6.2.2 Norepinephrine.

The variability in fragmentation by negative affect interaction was associated with norepinephrine levels (B = .027, p = .05). Increased variability in fragmentation was associated with increased norepinephrine at one standard deviation above the mean of negative affect (B = .038, p =.005), but there was no association at one standard deviation below the mean of negative affect (B =.002, p = .9) (Figure 7). The mean fragmentation by negative affect interaction was not associated with norepinephrine levels (B = .005, p = .4).

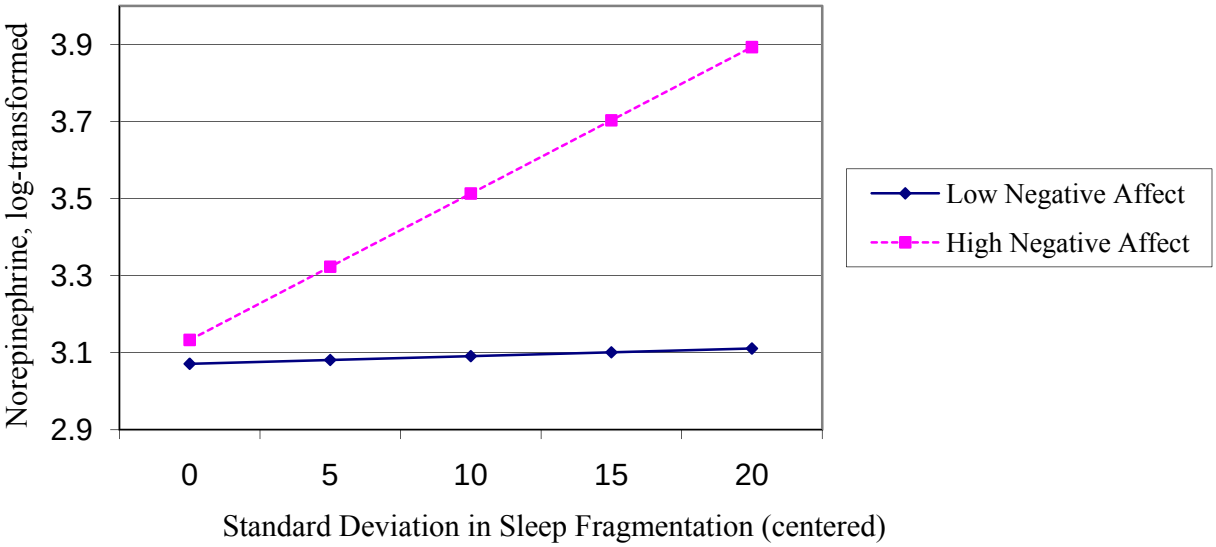


Figure 7. Simple Slopes of Norepinephrine on Intra-Individual Variability in Sleep Fragmentation at Low and High Levels of Negative Affect

7.0 DISCUSSION

The current study examined actigraph-measured sleep duration and fragmentation over nine nights in a sample of Black and White adults, with a particular interest in quantifying the amount of intra-individual variability in these parameters. A number of demographic and lifestyle factors were studied as potential correlates of variability in sleep patterns. Finally, the associations among sleep, mood, and sympathetic activity were examined, with the predictions that short, fragmented, and increasingly variable sleep would be associated with both higher levels of negative affect and higher nocturnal levels of urinary catecholamines.

The first aim of the study was to determine the degree of variability in individuals' sleep patterns over nine nights. The average night-to-night variation in sleep duration was slightly over an hour, which is similar to the standard deviation in duration across three nights reported by Knutson et al. (2007). A substantial portion of the variability in this sample appeared to be due to nightly differences in sleep onset, as bedtimes varied by approximately 45 minutes within individuals over the course of the study. The average nightly variation in the sleep fragmentation index was around 10, and morning diary ratings varied by .7 of a point. Moreover, all of these estimates, with the exception of diary ratings, were consistent whether examined over the first four or the last four nights of the study, suggesting that the variability was not due to the burden of sleep measurement equipment or random measurement error and instead may represent a trait-like tendency for unstable sleep. Unfortunately, however, nine nights of sleep measurement

assessed on one occasion do not provide sufficient data to conclude whether or not such variability truly represents a "stable" individual characteristic.

It was hypothesized that variation in sleep parameters due to differences within people would be greater than variation due to differences between people. To examine this prediction, multi-level modeling was used to determine the relative contributions of between- versus within-individual variation to the total unexplained variance in actigraphy measures, after accounting for the night of the week. Calculation of the intraclass correlation coefficient showed that 30% of the total variance in sleep duration was attributable to between-individual differences. An alternative interpretation of this statistic is that one could expect the within-individual correlation between any pair of sleep durations taken from the same individual to be approximately .30. Although this is a moderate correlation, it is clear that the majority of variability in sleep duration was due to within-individual differences. Between- versus within-individual differences for sleep fragmentation were not as clear cut, with 55% of the unexplained variance in fragmentation due to variability within individuals. However, both of these estimates support the hypothesis that adults have a considerable amount of nightly variability in their sleep, a factor which is often overlooked when studying the links between sleep and other health factors. From a methodological standpoint, it is clear that one or two nights of sleep measurement may not accurately represent an individual's habitual sleep patterns. If researchers are interested in capturing average estimates of sleep and estimating their "true" relationships with other variables, it is necessary to collect data over multiple nights. For instance, reliability analyses of the data show that a minimum of six nights and three nights of measurement would be necessary to obtain adequately reliable estimates of duration and fragmentation, respectively – figures which are consistent with or slightly lower than those that have been reported previously in the

literature (Acebo et al., 1999; Knutson et al., 2007; Wohlgemuth, Edinger, Fins, & Sullivan, 1999).

7.1 INTRA-INDIVIDUAL VARIABILITY IN SLEEP BY SEX AND RACE

It was hypothesized that the amount of variability in sleep would differ by sex and race; in specific, women and Blacks were expected to have more intra-individual variability in their sleep patterns than men and Whites, based on past findings. Indeed, women in the current sample had more intra-individual variability in sleep duration over nine nights compared to men, an effect which remained after adjustment for average hours of sleep. Increased variability in duration among women is particularly interesting in light of the fact that on average, women tend to sleep longer than men (Goel, Kim, & Lao, 2005; Ohayon et al., 2004), which was also the case in the current sample. Follow-up analyses suggested that this effect was partially driven by less consistent bedtimes among women, as sex differences in duration were eliminated after adjustment for variability in reported bedtimes (data not shown). Although a number of factors may be associated with increased variability in bedtimes and duration in women, seemingly obvious candidates such as employment status or number of stressful life events were not responsible for these findings. It is possible that women are more susceptible to a variety of other biological or psychological influences that affect the nightly timing of sleep but were not captured in this study. For example, factors such as physical symptoms, pain, or family demands may be more relevant for the timing of women's sleep, in particular, thereby affecting overall duration. There were no sex differences in intra-individual variability in sleep fragmentation, which is inconsistent with a previous report that women had greater variability in actigraphy

measures of movement than men (VanHilten et al., 1993). Measures of variability in the current study were based upon more nights of data as well as a different index of nocturnal movement, which may account for dissimilar results. Regardless, both the findings from the current study and those reported by VinHilten et al. (1993) suggest that women may have more variability in various sleep parameters than men, and the factors that are associated with such variability are worth further examination.

While a number of studies have found that Blacks tend to have shorter and more fragmented sleep compared to Whites (Jean-Louis, Kripke, Ancoli-Israel, Klauber, & Sepulveda, 2000; Lauderdale et al., 2006), little research has examined race differences in night-to-night variability in these parameters. In this sample, Blacks had more intra-individual variability in sleep fragmentation and bedtimes than Whites. Controlling for a number of psychosocial and behavioral variables, such as stressful events, employment status, and exercise, reduced the strength of the association between race and variability in sleep fragmentation, but it did not fully account for this finding. Moreover, none of the measured psychosocial or health variables were responsible for the increased variability in bedtimes among Blacks. One recent study also found that Blacks generally had more nightly variability in actigraph-measured sleep characteristics over three nights (Knutson et al., 2007); however, details regarding specific parameters were not reported, making direct comparisons between the two studies difficult. These findings may have methodological implications, particularly in light of the increasingly reported race disparities in sleep duration and fragmentation. If it is indeed true that Blacks have more nightly variability in their sleep, it may be especially important to collect multiple nights of data when examining race differences in sleep or when studying how such differences may be related to other health factors.

7.2 INTRA-INDIVIDUAL VARIABILITY IN SLEEP AND SELF-REPORTED SLEEP QUALITY

An additional purpose of the study was to examine the relationship between intra-individual variability in sleep and perceptions of sleep quality. Individuals who had greater nightly variability in sleep duration reported poorer sleep quality on the PSQI. Although average duration or fragmentation might typically be considered the dimensions most closely linked to self-reported sleep quality, a stronger association between variability and sleep quality was found in this study, with averaged sleep values unrelated to PSQI scores. At least two previous studies have reported a relationship between irregular sleep-wake schedules and daytime sleepiness (Billiard, Alperovitch, Perot, Jammes, 1987; Strauch & Meier, 1998), and Manber et al. (1996) showed that an intervention that stabilized sleep patterns resulted in less daytime sleepiness and better self-reported sleep quality (improvements which were independent of sleep duration). While the above studies were conducted in college students, a population in which irregular sleep-wake schedules are common and perhaps more severely disrupted, the current results show that the relationship between increased variability and poor sleep quality extends into adulthood. In the aggregate, these studies suggest that intra-individual variability in sleep patterns may be more strongly related to perceptions of sleep quality than average levels of duration or fragmentation.

A related hypothesis was that nightly deviations in sleep duration would be better predictors of morning ratings of sleep quality than absolute numbers of hours slept. In other words, it was predicted that it was not the amount of sleep an individual received, but how abnormal that amount was in relation to his or her average sleep duration, that would determine perceptions of sleep quality the subsequent morning. Initial analyses showed that longer sleep

was related to better sleep quality ratings; however, this association was eliminated when nightly deviation values were included in the model, demonstrating that a shorter sleep duration, relative to one's average, was more closely related to poor sleep quality. An interactive effect was also observed in which such deviations were stronger predictors of sleep quality in men than in women. A possible explanation for this finding is that the criteria used to evaluate subjective sleep quality vary between men and women. Although previous studies on sex differences in the factors associated with self-reported sleep quality have been mixed (McCrae et al., 2005), there is some evidence to suggest that the relationship between objectively measured sleep parameters and self-reported sleep quality is stronger in men than in women (Vitiello, Larsen, & Moe, 2004). Therefore, it is possible that duration or variability in duration of sleep were influential in men's evaluations of sleep quality, while other unmeasured factors were more salient for women.

Overall, these results highlight the potential impact that nightly decrements from one's average sleep duration have on perceptions of sleep quality and feelings of restfulness. Furthermore, the nature of the analyses helps to rule out the alternative possibility that poorer sleep quality might somehow lead to increased variability in nightly duration. Mechanisms that link irregular patterns of sleep duration to poor sleep quality and the moderating role of sex in these associations may be promising areas for future research.

7.3 INTRA-INDIVIDUAL VARIABILITY IN SLEEP AND PSYCHOSOCIAL/HEALTH FACTORS

In addition to quantifying intra-individual variability in sleep parameters, another aim of this study was to explore the associations between variability in sleep and a variety of psychosocial

and health factors. Individuals who reported that they were currently experiencing more life stressors had greater variability in both sleep duration and fragmentation, and these relationships were independent of average sleep parameters, sleep quality, demographics, and health factors. Although the causation of this relationship cannot be determined, it seems likely that ongoing, upsetting life events could lead to disruptions in one's daily routine, thereby affecting sleep-wake schedules. Investigation of how daily stressors influence different dimensions of sleep on a night-to-night basis is a related question that may be an important area for future investigation. Variability in sleep was unrelated to physical activity or BMI after adjustment for other relevant variables; however, an association between increased variability in fragmentation and less alcohol use was observed. The reason for this association is unclear; although moderate doses of alcohol have been shown to lead to increased wakefulness during the latter half of the night (Vitiello, 1997), no associations between alcohol use and nightly variability in sleep fragmentation have been reported.

7.4 SLEEP AND NEGATIVE AFFECT

It was hypothesized that both a short sleep duration and increased fragmentation would be associated with increased negative affect; however, there was no support for these relationships in this sample. It may be that associations between average sleep parameters and affect only exist at extreme ends of the spectrum, such as when sleep length is severely reduced or eliminated, or only within psychiatric samples. The fact that the strongest evidence supporting an association between sleep duration and negative affect comes from experimental studies in which either total or partial deprivation leads to changes in mood (Caldwell et al., 2004; Dinges

et al., 1997; Haack & Mullington, 2005; Kahn-Greene et al., 2007), with cross-sectional findings having produced less consistent results (Jean-Louis et al., 2000; Pilcher et al., 1997; Totterdell et al., 1994), supports this theory. Moreover, while objective indices of sleep fragmentation tend to be heightened in clinically depressed or anxious individuals (Armitage et al., 1997; Fuller et al., 1997; Korszun et al., 2002; Kupfer, 1995; Lemke et al., 1999), analogous data in non-clinical samples are lacking. The type of sleep measurement under study may also be an important factor, as the few observed relationships between mood and sleep have been based on self-reports of duration or sleep disturbances (Brissette & Cohen, 2002; Moffitt et al., 1991; National Sleep Foundation, 2002), as opposed to actigraphy or PSG.

Therefore, while the literature on average sleep duration, fragmentation, and mood remains inconclusive, the results from the current study suggest that average sleep parameters and negative affect are unrelated in a non-psychiatric sample free from sleep disorders. Future research in non-clinical samples may want to examine the possibility that sleep loss or fragmentation interferes with an individual's ability to effectively cope with discrete stressors (i.e., Zohar et al., 2005), rather than influencing reports of more general and chronic negative emotional traits. Additionally, recent research has highlighted the role of individual differences in the impact that sleep deprivation has on cognitive processes, with the suggestion that sufficient or "optimal" lengths of sleep may vary between individuals (Viole et al., 2007). Whether or not similar individual differences exist in the association between sleep duration and emotional responses may constitute another area for future work.

Neither intra-individual variability in duration nor fragmentation was associated with reports of negative affect when this relationship was examined within the full sample. Increased negative affect has been observed in adolescents who have variable sleep patterns or large

weekday-weekend discrepancies in their bedtimes (Fuligni & Hardway, 2006; Wolfson & Carskadon, 1998). The only reported association between sleep variability and mood in adults comes from an experiment in which the timing of individuals' sleep was manipulated over several nights (Taub & Berger, 1974). Although the current results do not offer much support for an association between intra-individual variability in sleep and negative affect, it is possible that such a relationship is stronger in or limited to specific developmental periods. For example, the variations in sleep-wake schedules that characterize adolescence, such as phase shifts and weekday-weekend discrepancies (Sadeh & Gruber, 2002; Wolfson & Carskadon, 1998), may be more profound than those found in adulthood, and the aspects of affect regulation that are believed to be developing in the pubertal period may be particularly vulnerable to the effects of inadequate or unstable sleep at that time (Dahl, 2002).

7.5 SLEEP AND NEGATIVE AFFECT BY SEX

Although intra-individual variability in sleep was not associated with negative affect in the full sample, stratification of the sample by sex revealed relationships between increased variability in both duration and fragmentation and negative affect in men but not women. Moreover, exploratory analyses showed that variability in these sleep parameters was most strongly associated with anxiety, as opposed to depressive symptoms or hostility, in men (data not shown). The reason for differential results within sexes is unclear. Although women had more intra-individual variability in duration and fragmentation on average, there was a wider range of values for both of these parameters in men, raising the possibility that those whose sleep variability fell at the high or low extremes may have been driving this effect. However, these

findings must be interpreted cautiously, as the interactive effects between sex and intra-individual variability in duration and fragmentation were not statistically significant and no *a priori* hypothesis existed as to why such associations would be found exclusively in men.

In sum, findings from the current study do not provide strong support for a relationship between variability in sleep and negative affect. However, when combined with past work, they suggest that additional research on the moderating effects of age and sex on the relationship between variability in sleep and negative affect may be warranted. It may also be the case that only relatively extreme disruptions in sleep patterns, such as the ones imposed by Taub and Berger's (1974) experiment, are related to alterations in mood.

7.6 SLEEP AND SAM ACTIVITY

It was predicted that short, fragmented, and variable sleep would be associated with increased nocturnal SAM activity, as measured by urinary catecholamine excretion. For the most part, actigraphy measures of average sleep and intra-individual variability in sleep were not associated with nocturnal catecholamine levels, with the exceptions being that increased variability in fragmentation was related to increased norepinephrine, and in men only, to increased epinephrine. If these findings indeed represent "true" effects, it may be that individuals whose sleep fragmentation varies from night to night have a less efficient decline in nocturnal sympathetic activity due to a desynchronization between sleep patterns and physiological systems, similar to the phenomenon observed in rotating shift workers (Bøggild & Knutsson, 1999; Totterdell, 2005). Alternatively, increased sympathetic activation at night may lead to disrupted sleep on a more variable rather than consistent basis. As discussed previously, it is

also possible that men whose fragmentation variability was very high were the most likely to have increased epinephrine levels. However, these explanations do not address the fact that catecholamine levels were not increased among those with more fragmentation; indeed, higher fragmentation tended to be associated with lower norepinephrine, a relationship opposite to the one predicted. Because multiple analyses were conducted and results were specific to norepinephrine or men only, the possibility of spurious associations must also be considered.

7.7 NEGATIVE AFFECT AS A MODERATOR OF SLEEP-SAM ACTIVITY ASSOCIATIONS

The final set of hypotheses proposed that associations between short, fragmented, or variable sleep and catecholamine levels would be stronger among individuals reporting high versus low levels of negative affect. As predicted, several interactive effects between negative mood and sleep parameters in relation to nocturnal catecholamine levels were observed. The interactions between negative affect and intra-individual variability in sleep parameters were the most consistent, such that increased variability in both duration and fragmentation tended to be associated with heightened epinephrine and norepinephrine levels in individuals high in negative affect. Interestingly, relationships between variability in sleep and catecholamines were in the opposite direction or absent among those reporting lower levels of negative affect. Similar, albeit less consistent, patterns emerged when examining the interactive effects of average sleep parameters and negative affect. A shorter sleep duration was associated with higher norepinephrine levels, and more fragmented sleep was associated with higher epinephrine levels, among individuals high in negative affect only.

Sleep deprivation has led to increased epinephrine and norepinephrine levels in experimental studies (Akerstedt, 1979; Froberg et al., 1972; Irwin et al., 1999; Steinberg et al., 1969), and fragmented sleep has been associated with increased norepinephrine in chronically stressed individuals and insomniac patients (Davidson et al., 1987; Irwin et al., 2003; Mausbach et al., 2006). Moreover, changes in shift work schedules also have been shown to cause changes in catecholamine excretion (Orth-Gomer, 1983; Theorell & Akerstedt 1976; Vokac, Magnus, Jebens, & Gundersen, 1981). Results from the current study demonstrate that associations between short, fragmented, or variable sleep and increased nocturnal catecholamines may also exist outside of experimental paradigms and among more normative populations when the moderating role of negative affect is taken into consideration. The fact that these relationships were only found in individuals who reported high levels of depression, anxiety, and hostility suggest that sleep and mood may act in a synergistic fashion to influence nocturnal SAM activity.

The mechanisms by which increased intra-individual variability in sleep is associated with SAM activity are unknown. One possibility is that chronic variability in sleep patterns leads to an inefficient decline of the SAM system among individuals high in negative affect. A highly variable sleep pattern may be common among individuals who are constantly trying to "catch up" to an optimal amount of sleep and therefore may reflect an underlying state of sleep deprivation. If sleep is considered to be a prolonged rest and physical recovery period, elevated catecholamine levels may represent a blunted or dysregulated nocturnal decline in sympathetic nervous system activity, and therefore constitute one pathway by which sleep and affect combine to influence disease risk. Of course, the relationships between these variables were cross-sectional in nature and several alternative explanations could account for the observed findings.

For example, heightened nocturnal activity of the SAM system could lead to unstable, disrupted sleep (i.e., Irwin, 1999), and these two factors could act separately or in tandem to influence daytime negative affect. Nighttime SAM activity and disrupted sleep patterns could also both be due to an underlying disease state.

7.8 LIMITATIONS & STRENGTHS

There are several limitations to the current study that must be considered when interpreting the above results. First, although actigraphy and sleep diary data were collected over nine nights, which is an improvement over past studies, nearly half of these nights involved the additional burden of PSG or blood pressure equipment. A more prolonged study period in which only actigraphy assessments were collected would provide "cleaner" and more generalizable data for examining the proposed hypotheses. Second, the daily factors associated with changes in sleep duration or fragmentation were not characterized. While the current results inform our understanding of how sleep patterns relate to psychosocial factors in general, future research may want to focus on how sleep co-varies with such factors on a day to day basis. Such a study design would also help clarify the causal question of whether sleep loss has a stronger influence on daily stressors, or vice versa. A related limitation is the cross-sectional nature of the current study. As mentioned above, causal relationships between sleep parameters and other variables such as sleep quality, stressful life events, or SAM activity cannot be determined based on the current findings. Finally, multiple statistical analyses were conducted and some of the reported interactions did not reach statistical significance. The fact that all of the interactive effects

between sleep and negative affect followed the same pattern suggests that this was most likely a power issue; however, the possibility of an inflated Type I error must also be considered.

This study also has several strengths, the first of which is the use of actigraphy to obtain valid, non-invasive measurements of sleep duration and fragmentation in participants' homes for an extended period of time. The relatively large sample size included both Black and White participants who were free from potentially confounding disorders, such as heart disease, diabetes, and sleep disorders. A wide range of psychosocial and behavioral health variables, such as negative affect, stressful life events, physical activity, and alcohol and nicotine use, were collected, making it possible to not only study their independent associations with sleep parameters, but also allowing for potentially relevant confounding factors to be controlled for in analyses. Finally, the investigation of intra-individual variability in duration and fragmentation represents an understudied and unique aspect of sleep research that attempts to take advantage of multiple assessments, rather than collapsing data into averages.

7.9 SUMMARY OF FINDINGS: A PROPOSED MODEL OF SLEEP AND PSYCHOLOGICAL AND PHYSIOLOGICAL FACTORS

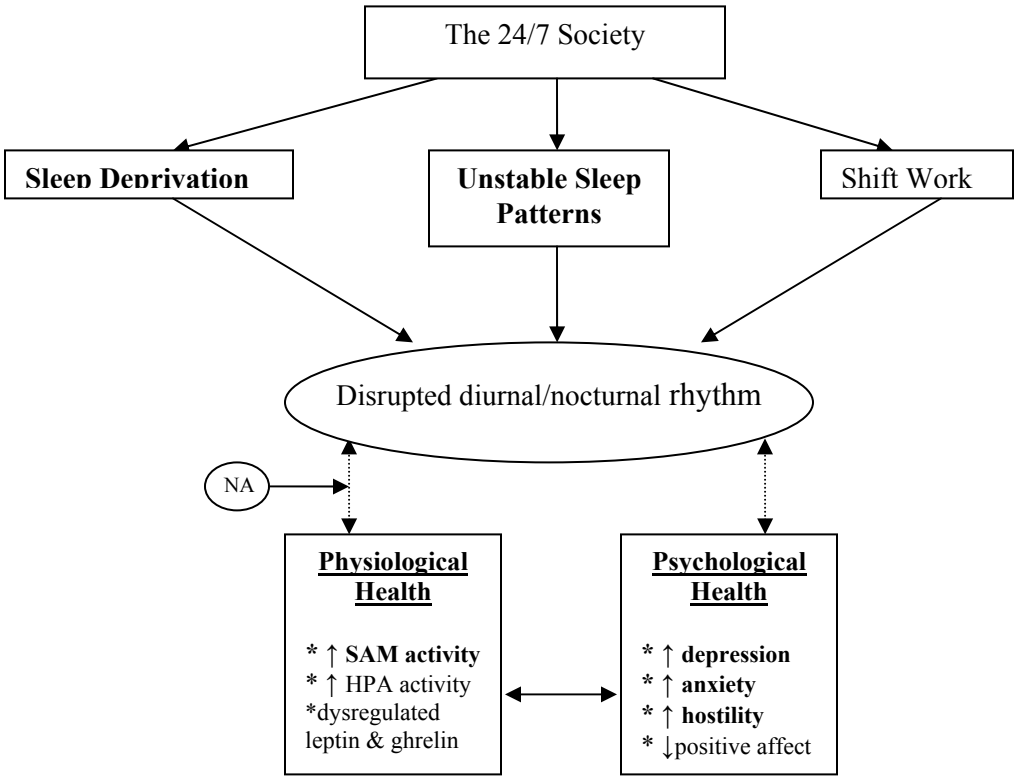
The findings from the current study can be discussed in the context of a model recently presented by Pickering (2006), which identifies hypothesized pathways by which irregular sleep leads to chronic disease. Pickering posits that shorter sleep durations and shift work have become commonplace in what he terms a "24/7 society." In the original model, chronic sleep deprivation and shift work are factors that can be characterized as part of an overall disruption of the diurnal rhythm of sleep and wakefulness. It has been posited that this dysregulation of sleep and

wakefulness results in a variety of physiological disturbances, such as increased SAM activity and activation of the hypothalamic-pituitary axis, which in turn increase risk for a number of disease outcomes, including obesity, diabetes, and cardiovascular morbidity.

A version of the model adapted for the current study is presented in Figure 8, with the factors that were investigated highlighted in bold. The adapted model suggests that, in addition to sleep deprivation and shift work, irregular sleep patterns may also be the result of a "24/7 society." Indeed, the current study provides evidence that substantial intra-individual variability in sleep duration, in particular, exists, and suggests that such variability may be an additionally important contributing factor to a dysregulated diurnal/nocturnal rhythm. Moreover, variability in sleep patterns may differ by sex and race, and it appears to be associated with factors such as self-reported sleep quality and stressful life events.

The model is also expanded to include psychological as well as physiological health outcomes. In other words, it was posited that dysregulation of the diurnal/nocturnal rhythm, as characterized by short sleep duration, increased fragmentation, and increased variability, would lead to both increased negative affect and heightened nocturnal SAM activity. The current study found little support for an association between negative affect and sleep; however, there was some evidence for a relationship between intra-individual variability in sleep and increased negative affect in men only. Finally, the links between dimensions of sleep and nocturnal catecholamines were either inconsistent or lacking when examined in isolation, but it appeared that negative affect moderated these relationships. Individuals who had short, fragmented, or increased variability in their sleep, and who reported increased anxiety, hostility, and depressive symptoms, were more likely to have heightened nocturnal SAM activity than those who had less disrupted sleep and reported lower levels of negative affect. While it is possible that sleep

disruptions caused an inefficient decline of the SAM system during the night in individuals high in negative affect, the cross-sectional nature of these associations must be kept in mind.



Adapted from Pickering (2006). Factors in bold represent variables that were investigated in the current study. Solid lines represent associations that were supported in the current study or have been supported by past research. Dashed lines represent associations that were found to be inconsistent or moderated by other factors in the current study. NA = negative affect.

Figure 8. A Proposed Model of Sleep and Psychological and Physiological Factors

8.0 BIBLIOGRAPHY

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