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Intra-Individual Variability in Sleep Duration and Fragmentation: Associations with Stress

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Summary

Despite growing evidence that there is substantial nightly, intra-individual variability in sleep duration and fragmentation, few studies have investigated the correlates of such variability. The current study examined whether intra-individual variability in sleep parameters was associated with psychosocial and physiological indices of stress, especially among those high in negative affect. Participants were 184 adults aged 46–78 (53% men, 41% Black) participating in the Pittsburgh SleepSCORE study. Wrist actigraphy was used to estimate sleep duration and fragmentation for nine nights, and overnight samples of urinary norepinephrine were collected for two nights. Stressful life events, depression, and anxiety were also reported. Intra-individual differences exceeded between-person differences in actigraphy-measured sleep duration and fragmentation. Stressful life events were associated with increased nightly variability in duration and fragmentation ($ps < .05$). Negative affect moderated associations between norepinephrine and variability in sleep, such that the greatest variability in actigraphy measures was among those with both high norepinephrine levels and high negative affect ($ps < .05$). These data suggest that both psychosocial and physiological stress are related to increased nightly variability in individuals' sleep duration and fragmentation, particularly among those reporting negative emotions. These results may have implications for both sleep and health research.

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Ms. Mezick designed the present study, wrote multiple drafts of the manuscript, and performed the statistical analysis. Dr. Matthews was the PI for SleepSCORE, interpreted data, and contributed to multiple drafts of the manuscript. Dr. Hall contributed to multiple drafts of the manuscript and helped with data interpretation. Dr. Kamarck contributed to multiple drafts of the manuscript and helped with data interpretation. Dr. Buysse contributed to multiple drafts of the manuscript. Dr. Owens contributed to multiple drafts of the manuscript. Dr. Reis contributed to multiple drafts of the manuscript. Dr. Matthews, Dr. Hall, Dr. Kamarck, Dr. Owens, Dr. Buysse, and Dr. Reis each contributed to the study design and protocol. All of the authors contributed to and approved the final manuscript.

Conflict of Interest Disclosure

Dr. Daniel Buysse serves as a consultant for Actelion, Arena, Cephalon, Eli Lilly, GlaxoSmithKline, Merck, Neurocrine, Neurogen, Pfizer, Respiromics, sanofi-aventis, Sepracor, Servier, Somnus Therapeutics, Stress Eraser, Takeda and Transcept Pharmaceuticals, Inc. Dr. Martica Hall was paid for a presentation on sleep in women at a conference sponsored by Highmark Blue Cross. No other author reports a conflict of interest.

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Keywords

intra-individual variability; sleep; actigraphy; stress; norepinephrine; negative affect

Introduction

Accumulating evidence shows there is considerable intra-individual variability in sleep, with estimates of within-person differences exceeding differences between persons in measures of duration and fragmentation (van Hilten et al., 1993; Tworoger et al., 2005; Knutson et al., 2007). Findings linking sleep and morbidity are typically based upon averages or single-night assessments of duration or fragmentation. However, given the substantial nightly variability in such parameters, this component may also be important to consider. Importance of variability in sleep for health is consistent with findings showing increased rates of disease among individuals employed in rotating shift work, and adjustments in shift work schedules altering physiological responses such as catecholamine excretion (Vokac et al., 1981; Orth-Gomer, 1983). Understanding the determinants of variability in sleep that is not imposed by shift work may have implications for both sleep and health research. Here, we focus on the relationship between stress and nightly variability in individuals' sleep duration and fragmentation.

Both psychosocial and physiological indices of stress are associated with sleep disturbances. Stressful life events precede and accompany decreases in sleep duration and increases in fragmentation (Healey et al., 1981; Sadeh et al., 2004; Lee et al., 2007; Vahtera et al., 2007; Hall et al., 2008), and elevated levels of nocturnal catecholamines, particularly norepinephrine, are apparent in individuals with highly fragmented sleep (Davidson et al., 1987; Vgontzas et al., 1998; Irwin et al., 2003; Mausbach et al., 2006). These findings are based on either a single night of sleep or averages across nights. It is reasonable to suggest that heightened physiological and self-reported psychosocial stress also may be related to irregularity in sleep from night to night. As an example, an individual who experiences stress may have short and fragmented sleep on one night, but due to sleep deprivation and sleepiness, the individual may sleep longer and more solidly on the next night. Thus, stress may be associated with variability in sleep duration and fragmentation, independent of average values of these parameters. Such a pattern would be consistent with homeostatic sleep regulation, in which deficient sleep leads to compensatory increases in sleep duration and depth, while excessive sleep results in the opposite effect.

Negative emotions are often reported by individuals undergoing stressful life events (Boyce et al., 1998; Tesser and Beach, 1998), and they are also associated with increased catecholamine levels (Janicki-Deverts et al., 1998; Musselman et al., 1998). Moreover, negative emotions and depression are related to shorter sleep duration and greater fragmentation (Armitage et al., 1997; Fuller et al., 1997; Kaneita et al., 2006), although not all studies find such links (Totterdell et al., 1994; Pilcher et al., 1997). Given these relationships, it may be that those individuals most sensitive to stress - i.e., those who report high negative affect - are most likely to show associations between variability in sleep and stress. The objectives of the current study are to examine intra-individual variability in actigraphic measures of sleep duration and fragmentation across nine nights, and to test whether such variability is related to psychosocial and physiological indices of stress. We hypothesize that increased variability in actigraphy measures of sleep are associated with increased stressful life events and increased nocturnal norepinephrine levels, especially among individuals who report high levels of negative affect. We also expect that nightly differences within individuals exceed differences between individuals in both duration and fragmentation, as has been reported previously (van Hilten et al., 1993; Tworoger et al., 2005; Knutson et al., 2007).

Methods

Participants were recruited from the Heart Strategies Concentrating On Risk Evaluation (HeartSCORE) 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 HeartSCORE 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 ± 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).

The sleep study, entitled SleepSCORE, enrolled approximately equal ratios of male to female and Black to White participants from the HeartSCORE study sample. HeartSCORE participants were excluded if they were being treated for sleep-disordered breathing using continuous positive airway pressure or if they took medications for sleep on a regular basis. Other SleepSCORE exclusionary criteria included pregnancy; nighttime work schedule; medication for diabetes; and prior diagnosis of stroke, myocardial infarction, or interventional cardiology procedures. Participants who were observed to have sleep-disordered breathing during the course of the study were not excluded, and their data were retained. Other sleep disorders (insomnias, parasomnias) were not assessed for recruitment or exclusionary purposes. The present report is based on the first 187 participants who completed the study out of the target of 225 participants.

Measures and Procedure

Overview—Participants were recruited during HeartSCORE 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 approximately three months of obtaining consent. The study protocol lasted 10 days (for a complete description of the study protocol, see Matthews et al., 2008). 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. Overnight levels of urinary catecholamines were collected over 15-hour periods on nights 2 and 4. Two nights of PSG recording were conducted in participants' homes (nights 1 and 2). On the first night, participants were monitored for sleep-disordered breathing using nasal pressure, inductance plethysmography, and fingertip oximetry.

Actigraphy—Participants wore an Actiwatch-64 (Respironics, Inc., Bend, Oregon) on the non-dominant wrist continuously for 9 nights and 10 days. Data were stored in 1-minute epochs and validated MiniMitter software (Respironics, Inc.) algorithms were used to estimate sleep parameters. The two actigraphy variables considered in analyses were assumed sleep duration and fragmentation index. Assumed sleep duration is the length of time between the actigraph-estimated sleep start and end times and does not subtract actigraph-identified awakenings throughout the night. Therefore, it is an estimate of general sleep-wake patterns and is less highly associated with sleep fragmentation than a variable such as total sleep time. The fragmentation index is a measure of nocturnal movement calculated as follows: ((number of

mobile epochs lasting four epochs + number of immobile epochs < 1 minute duration/number of immobile epochs > 1 minute duration) $\times$ 100), with higher levels of fragmentation indicating worse sleep continuity. In the SleepSCORE sample, the fragmentation index was highly correlated with actigraphy sleep efficiency ($r = -.77, p < .001$). Mean estimates for assumed sleep duration and the fragmentation index were obtained by averaging the nine values from each night of the study. Estimates of intra-individual variability in duration and fragmentation were obtained by calculating the standard deviation (SD) in these parameters over the nine nights for each individual.

Polysomnography—Two nights of PSG recording were conducted in participants' homes using a Compumedics Siesta monitor. The PSG montage included bilateral central and occipital electro-encephalogram channels, bilateral electro-oculograms, bipolar submentalis electromyograms, and one channel of electrocardiogram recording. On the first night of PSG, participants were monitored for sleep-disordered breathing using nasal pressure, inductance plethysmography, and fingertip oximetry. Trained PSG technologists scored sleep records. American Academy of Sleep Medicine Task Force (1999) definitions were used to identify apneas and hypopneas; oximetry readings were used to quantify average and minimum oxygen saturation levels. The apnea-hypopnea index (AHI) was used as a covariate in analyses.

Stressful Life Events—Stressful life events were assessed using two measures created for this study. The first, a modified version of the Psychiatric Epidemiology Research Inventory Life Events Scale (Dohrenwend et al., 1978; Dohrenwend and Dohrenwend, 1981) asked participants to indicate whether they had experienced any of 19 negative life events (e.g., “a close relative died,” “legal problems or problems with police”) during the past six months and whether or not the event was perceived as “still upsetting.” The number of items endorsed as “still upsetting” was added to create a total count of current stressful events. The second measure assessed whether participants were currently experiencing a number of chronic, ongoing stressors (“ongoing health problems,” “ongoing financial strain”) and how stressful the problems were on a 1 to 3 (“not very stressful” to “very stressful”) scale. The number of ongoing problems that were endorsed as “very stressful” was added to create a total count of chronic and ongoing stressors. Due to conceptual overlap between the two scales and the fact that they were significantly correlated with each other ($r = .40, p < .001$), total scores from each were standardized and then averaged to create a current life stressors composite score. Because only items that were endorsed as “still upsetting” or “very stressful” were included in the total score, this variable was meant to capture the perceived severity of stressors rather than simply the number of life events that had occurred.

Norepinephrine—Norepinephrine levels 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 were kept on ice until samples were aliquotted and frozen in the laboratory. Norepinephrine levels were determined by high performance liquid chromatography with electrochemical detection and corrected for urine volume. Sensitivity was 1.33 ng/ml, and the between-assay variation ranged from 8.5–14.0%. None of the participants had elevated creatinine > 1.5 mg/dl. Mean norepinephrine was calculated by averaging the levels obtained from the two nights of collection (correlation across the two nights: $r = .47, p < .001$). Due to skewness, this value was log-transformed before use in analyses. Norepinephrine levels were positively associated with stressful life events in this sample ($r = .17, p = .03$). The relatively weak association between these two factors suggests that although they are related, there are most likely additional influences on norepinephrine release (e.g., unmeasured psychological stressors, smoking, caffeine use). We also measured

epinephrine levels in this sample but do not report the results herein because they were not associated with stressful life events ($r = -.04$, $p = .60$) or any sleep measures ($ps > .20$).

Negative Affect—We conceptualized negative affect as a general disposition to experience negative emotionality as measured by questionnaires of depressive symptoms and anxiety. The Center for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977) was used to measure depressive symptoms, and the sleep item was excluded from the total score. Although the CES-D inquires about symptoms over the past week, we have observed the test-retest reliability of this measure to remain fairly stable over a period of one year in other data sets (average $r = .50$ across eight annual assessments). Trait anxiety was assessed using the Spielberger Trait Anxiety Inventory (STAI), a measure which has good stability over time in adult samples (Spielberger et al., 1970; Barnes et al., 2002). There is support for both conceptual and theoretical overlap between the constructs of depression and anxiety (Watson et al., 1995; Suls and Bunde, 2005), and CES-D and STAI scores were correlated at $r = .38$ ($p < .001$) in the current study. Scores from the two measures were standardized, and these values were averaged to create one continuous variable indicating negative affect.

Covariates—Covariates for analyses included race, sex, age, BMI, AHI, and cardiac/hypertensive medication use, due to their potential associations with sleep and/or indices of stress. Race, sex, and age were determined by self-report. Body mass index (BMI) was assessed in the HeartSCORE study protocol. Reports of daily medication use were collected during in-home interviews. AHI was defined as number of apneas and hypopneas per hour of sleep, using the American Academy of Sleep Medicine Task Force (1999) definitions. The four medications associated with sleep and/or norepinephrine levels in this sample were angiotensin-II receptor blockers, angiotensin-converting enzyme inhibitors, alpha-1 blockers, and alpha-2 agonists. Use of any one of these four medications was coded dichotomously (“yes/no”) and included as a covariate. We also measured self-reported history of depression and generalized anxiety disorder, antidepressant use, and nicotine use. As only a small percentage of the sample reported a history of clinical depression (10.3%) or anxiety (4.9%), were taking antidepressants (8.7%), or were smokers (10.3%), and their inclusion as covariates did not change the results reported below, we did not include them in statistical models.

Statistical Analysis

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 statistical 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 not included in analyses. Therefore, total sample sizes for analyses involving sleep duration and sleep fragmentation were 184 and 183 participants, respectively.

The first set of analyses focused on quantifying intra-individual variability in sleep duration and fragmentation, and describing any race and sex differences in these parameters. Multi-level modeling was used to determine the proportion of total variance attributable to within-individual differences and between-individual differences in assumed sleep duration and sleep fragmentation. 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, as individuals slept longer and tended to have less fragmented sleep on weekends than weekdays, ($t = 2.16$, $p = .03$; $t = 1.37$, $p = .10$, respectively). 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 covariance was used to examine differences in intra-individual variability in sleep duration and fragmentation by sex and race groups after adjustment for covariates.

We examined the associations between indices of stress and variability in sleep in a series of linear regression models. Stressful life events and norepinephrine levels each were entered in separate models as predictors of nightly variability in duration and fragmentation. Centered covariates included age, sex, race, BMI, AHI, and medication use, as well as the relevant mean sleep parameter to test if relationships were independent of average sleep (i.e., analyses using intra-individual variability in sleep duration as the outcome were adjusted for mean sleep duration). We then tested whether the associations between stress and sleep were stronger among individuals experiencing high levels of negative emotions by entering the stress variable (either life events or norepinephrine) and negative affect in the first step of the model, and the interaction between the two factors in the second step. Finally, as it is possible that PSG recordings may have contributed to increased variability in sleep parameters, we repeated the analyses of stress and sleep using only the data from nights 3–9 (nights on which PSG was not performed).

Results

Sample Characteristics

Table 1 displays descriptive information regarding demographics, psychosocial factors, and norepinephrine 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).

Intra-Individual Variability in Sleep Duration and Fragmentation

Table 2 displays descriptive information regarding means and intra-individual variability in sleep parameters for the entire sample, as well as by race and sex group. Intra-individual variability in sleep duration ranged from 18.6 – 214.5 minutes, and variability in the fragmentation index ranged from 2.6 to 27.8. After controlling for covariates and mean sleep parameters, Blacks had more individual variability in sleep fragmentation than Whites, and women had more individual variability in sleep duration than men. Age, BMI, AHI, and medication use were not related to variability in either sleep parameter ($ps > .1$), with the exception of a trend between increased apnea-hypopnea and increased variability in fragmentation ($\beta = .13, p = .08$). This association was no longer significant after adjusting for mean fragmentation ($\beta = .07, p = .30$).

An intercept-only multi-level model showed that the estimated between-person variance in sleep duration across nine nights was .63, and the estimated within-person variance was 1.53, after controlling for the number of weekday versus weekend nights in the study period. The ICC was calculated as .30, indicating the proportion of total variance over study days attributable to between-individual differences (conversely, 70% of the variance was attributable to differences 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 118.08, and the variance within individuals was 134.94. The ICC for the fragmentation index was .45.

Indices of Stress and Intra-Individual Variability in Sleep

Sleep Duration—Results from linear regression models testing the associations between psychosocial and physiological stress and variability in sleep duration are shown in Table 3. Reporting more stressful life events was associated with increased individual variability in

sleep duration after adjustment for mean sleep duration and covariates. There was no association between norepinephrine and variability in duration. Neither stressful life events nor norepinephrine was associated with average sleep duration ($ps > .50$).

Sleep Fragmentation—Results from linear regression models testing the associations between psychosocial and physiological stress and variability in sleep fragmentation are shown in Table 3. Reporting more stressful life events was associated with increased individual variability in sleep fragmentation after adjustment for mean fragmentation and covariates. Higher norepinephrine levels were also related to increased individual variability in fragmentation. When stressful life events and norepinephrine were included as predictors in the same model, they remained marginally associated with variability in fragmentation ($\beta = .12, p = .07$ for stressful life events; $\beta = .13, p = .06$ for norepinephrine).

Interaction of Stress and Negative Affect in Relation to Actigraphy Measures—Results from linear regression models testing the interactions between stress and negative affect as predictors of variability in sleep are also shown in Table 3. The life events X negative affect interaction was not associated with variability in duration, but it was associated with variability in fragmentation. Plotting the simple slopes at one SD above and below the mean of negative affect (e.g., Dearing and Hamilton, 2006) showed that an increased number of stressful life events was related to increased variability in fragmentation at high levels of negative affect, but there was no relationship at low levels of negative affect (Figure 1). The interaction between norepinephrine and negative affect was associated with variability in duration, and it also was associated with variability in fragmentation. Plotting the simple slopes of the interactive effects revealed that the relationships between norepinephrine and variability in sleep were positive at high levels of negative affect and negative or absent at low levels of negative affect (Figures 2 and 3).

Supplemental Analyses: Nights 3–9—We repeated the analyses examining the association between stress and variability in sleep after excluding data from PSG recording nights. Analyses using variability in sleep duration across nights 3 – 9 as an outcome produced similar results to those reported above (stressful life events: $\beta = .20, p = .006$; norepinephrine X negative affect: $\beta = .14, p = .07$; all other predictors: $ps > .4$).

Regarding sleep fragmentation, stressful life events were no longer related to variability in fragmentation after excluding PSG nights ($\beta = .07, p = .26$). The effects of interactive terms in relation to sleep fragmentation were unchanged (stressful life events X negative affect: $\beta = .17, p = .01$; norepinephrine X negative affect $\beta = .16, p = .01$). These analyses suggest that, for the most part, associations between stress and sleep variability appear to be independent of PSG measurement.

Discussion

In this study we investigated intra-individual, nightly variability in dimensions of sleep and tested whether this variability was related to psychosocial and physiological markers of stress. Consistent with past findings (van Hilten et al., 1993; Tworoger et al., 2005; Knutson et al., 2007), we observed that the majority of variability in sleep duration and fragmentation was due to within-individual as opposed to between-individual differences. From a methodological standpoint, these results suggest that one or two nights of sleep measurement may not accurately represent an individual's habitual sleep patterns. Thus, relationships between sleep and other variables may appear weak or null if statistical tests are based upon an inadequate number of sleep measurements across nights. In addition, nightly variability in sleep differed by demographic group, such that Blacks had more intra-individual variability in their sleep fragmentation than Whites, and women had more intra-individual variability in their sleep

duration than men, even after adjustment for mean sleep parameters. These results are consistent with findings from past studies (van Hilten et al., 1993; Knutson et al., 2007), suggesting that more research on race and sex differences in sleep variability is warranted, particularly in light of the increasingly reported demographic disparities in sleep (Lauderdale et al., 2006; Mezick et al., 2008; Nunes et al., 2008). Also noteworthy is that our study population was older than those in similar studies of variability (Knutson et al., 2007; Tworoger et al., 2005). Given the decreases in sleep duration and continuity that occur across the lifespan (Ohayon et al., 2002), nightly variability might also be expected to change with age. Both our study and at least one other failed to find a relationship between age and variability in sleep in older adults (van Hilten et al., 1993), but whether or not differences exist across wider age ranges (i.e., young, middle, and older-aged adults) is an interesting question for future work.

We found that individuals who were experiencing more negative life stressors had greater variability in sleep duration and fragmentation, and these relationships were independent of average sleep parameters, health factors, and demographics. Although the causation of these associations cannot be determined, it is plausible that ongoing, upsetting life events may disturb the consistency of sleep-wake schedules. For example, life stressors and their associated emotional responses might interfere with sleep length or continuity on one night via increased cognitive arousal or disrupted daytime patterns, resulting in relatively longer and more consolidated sleep the next night due to a homeostatic rebound effect. The fact that the link between life events and variability in sleep fragmentation was stronger among individuals reporting high levels of negative affect may suggest that those who are most susceptible to the negative effects of stress are most likely to experience sleep disruptions. Given the cross-sectional nature of the data, an alternative explanation is that variability in sleep patterns may result in more life stressors or an appraisal style in which events are perceived as more negative.

Data examining variability in sleep and nocturnal norepinephrine were somewhat less consistent than the data for life stressors, as higher norepinephrine was associated with increased variability in fragmentation, but not duration. Interactive effects showed that individuals with the greatest variability in actigraphy measures of sleep were those who had both elevated levels of nocturnal norepinephrine and high levels of depression and anxiety. A potential interpretation of these findings is that physiological stress, as indexed by heightened nocturnal activity of the sympatho-adrenal medullary system, leads to unstable and disrupted sleep patterns. The fact that associations between variability in sleep and norepinephrine were only found in individuals reporting elevated negative affect raises the possibility that emotions may exacerbate or buffer the associations between physiological stress and sleep patterns. Similar support for a moderating role of negative emotions on the links between stress hormones and physical health was reported in a recent paper by Wrosch et al. (2008), in which cortisol secretion was related to self-reported physical symptoms, but only among individuals who also experienced high negative affect. As the current analyses were cross-sectional, it is also possible that irregularity in sleep duration and repeated awakenings across nights may lead to a blunted decline of sympathetic activity at night, especially when compounded by negative emotional experiences. Others have found that poor sleep continuity is related to increased norepinephrine in insomniacs or individuals under chronic stress (Davidson et al., 1987; Vgontzas et al., 1998; Irwin et al., 2003; Mausbach et al., 2006), suggesting that links between sleep and catecholamines might only be apparent when sleep disturbances or stress levels are at their most extreme.

Of interest is the absence of a relationship between mean actigraphy measures and stressful life events. Although average sleep length or fragmentation are studied most often for their potential links with stress, stronger associations were found between variability in these measures and life stressors in the current study. Others have reported associations between irregular sleep schedules and poor sleep quality in non-clinical samples (Billiard et al., 1987)

or have observed more variability in sleep patterns among insomniacs as compared to controls (Wohlgemuth et al., 1999). In conjunction with the current findings, these studies suggest that nightly variability may be an important way to examine relationships between sleep and other variables in addition to more commonly used averages. It also may be interesting to study whether particular aspects of sleep or consequences of sleep loss are more trait-like than others, and, thus, have differential relationships with factors such as stress. For example, slow wave sleep and delta power show greater stability within individuals across both baseline and sleep deprivation experimental conditions than duration and continuity parameters (Tucker et al., 2007).

There are several limitations to the current study, including the cross-sectional nature of the data. As mentioned above, causal relationships between sleep parameters, indices of stress, and negative affect cannot be determined based on the current results. Analyses focused on estimated sleep duration, which is derived from patterns of movement only, and, therefore, is not synonymous with physiological sleep time. Although norepinephrine is often considered to be a physiological marker of stress (Goldstein, 2003), other factors, such as caffeine, nicotine use, and medications, are known to influence its release. However, we were able to statistically adjust for several of these variables. Another limitation is that our sample was recruited from a large study of volunteers in the Pittsburgh community screened for cardiovascular risk, and, therefore, does not represent the general population. In particular, patterns of variability and relationships between stress and sleep may vary in sample populations of different ages and psychiatric profiles, as the associations between these factors and sleep are well-established. Finally, stress and negative affect were conceptualized as trait-like constructs and measured as averages, as opposed to examining the variability of these measures across days. Future research may want to investigate whether daily fluctuations in affect also are related to variability in sleep.

The strengths of the study include the use of actigraphy to obtain non-invasive measurements of sleep duration and fragmentation in participants' homes for an extended study period and the ability to assess sleep-disordered breathing. The relatively large sample size included both Black and White participants who were free from heart disease, stroke, and diabetes. Finally, the investigation of intra-individual variability in duration and fragmentation is an understudied and unique aspect of sleep research that attempts to take advantage of multiple assessments, in addition to more commonly used averages.

In sum, intra-individual, nightly differences exceed inter-individual differences in actigraphy sleep duration and fragmentation. Reports of stressful life events are associated with increased intra-individual variability in sleep duration and fragmentation, independent of mean values of these parameters. Elevated overnight norepinephrine levels among individuals with variable sleep and negative emotions may represent a blunting of the nocturnal decline in sympathetic activity, and constitute one pathway by which sleep and affect combine to influence disease risk. The determinants and consequences of intra-individual variability in sleep may represent an important avenue for future sleep research.

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Abbreviations

HeartSCORE

Heart Strategies Concentrating on Risk Evaluation

SleepSCORE

Sleep Strategies Concentrating on Risk Evaluation

PSG

polysomnography

SD

standard deviation

AHI

apnea-hypopnea index

CES-D

Center for Epidemiological Studies Depression Scale

STAI

Spielberger Trait Anxiety Inventory

ICC

Intraclass correlation coefficient

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Figure 1.

Reporting increased number of stressful life events was associated with increased variability in sleep fragmentation at one standard deviation above the mean of negative affect ($\beta = .27$, $p = .002$). There was no association between stressful life events and variability in sleep fragmentation at one standard deviation below the mean of negative affect ($B = -.07$, $p = .47$).

Figure 2.

Increased norepinephrine was associated with increased variability in sleep duration at one standard deviation above the mean of negative affect ($\beta = .19$, $p = .05$). There was no association between norepinephrine and variability in duration at one standard deviation below the mean of negative affect ($\beta = -.10$, $p = .33$). Note: Norepinephrine values used in figure are log-transformed.

Figure 3.

Increased norepinephrine was associated with increased variability in sleep fragmentation at one standard deviation above the mean of negative affect ($\beta = .28$, $p = .002$). There was no association between norepinephrine and variability in sleep fragmentation at one standard deviation below the mean of negative affect ($\beta = -.03$, $p = .79$). Note: Norepinephrine values used in figure are log-transformed.

Table 1
Sample Characteristics

Variable	n (%)	M (SD)	Range
Sex			
Men	97 (52.7)		
Women	87 (47.3)		
Race			
White	105 (57.1)		
Black	75 (40.8)		
Asian	4 (2.1)		
Cardiac/Hypertensive Medication Use ^a	50 (27.2)		
Age		59.5 (7.2)	46 – 78
Body Mass Index		29.5 (5.0)	17.9 – 45.3
Apnea-Hypopnea Index		14.0 (15.5)	0 – 92.9
< 15 apneas/hypopneas per hour	128 (69.6)		
Still Upsetting Life Events		.7 (1.2)	0 – 5
Chronic, Ongoing Stressors		.4 (.9)	0 – 4
Norepinephrine ng/ml		35.0 (21.8)	4.3 – 110.3
CES-D Score ^b		10.9 (9.9)	0 – 40
STAI Score		6.0 (5.0)	0 – 21
Current Smokers	19 (10.3%)		
Current Antidepressant Use ^a	16 (8.7%)		

^aThese categories includes those who answered “yes” to cardiac/hypertensive or antidepressant medication use.

^bCES-D scores displayed in the table include the sleep item (#11); however, this item was excluded from the total score before use in analyses.

Unadjusted Means (SDs) and Night-to-Night Intraindividual Variability (SDs) in Sleep Parameters for the Total Sample and by Race and Sex Group

Variable	Race			Sex	
	Total Sample	Black n = 77	White n = 110	Men n = 99	Women n = 88
<u>Sleep Duration</u>					
Mean Assumed Sleep Time (min)	401.9 (53.9)	381.1 (53.3) ***	416.1 (49.8) ***	397.4 (54.8) *	406.8 (52.8) *
<u>Intraindividual Variability in Assumed Sleep Time (min)</u>					
	67.3 (28.7)	73.4 (27.3)	63.0 (28.9) *	63.0 (27.6) *	72.0 (29.2) *
<u>Sleep Fragmentation</u>					
Mean Fragmentation Index	32.6 (11.6)	35.6 (13.0) ***	30.5 (10.0) ***	33.9 (10.5) **	31.1 (12.6) **
Intraindividual Variability in Fragmentation Index	10.6 (4.8)	12.4 (4.9) ***	9.3 (4.4) ***	10.1 (4.3)	11.0 (5.3)

Note: Intraindividual variability values represent the standard deviation in an individual's sleep parameter over nine nights.

* $p \leq .05$ after adjustment for sex, race, age, BMI, apnea-hypopnea index, medication use, and the relevant mean sleep parameter.

** $p \leq .01$ after adjustment for covariates

*** $p \leq .001$ after adjustment for covariates.

Table 3

Associations between Indices of Stress and Variability in Sleep Duration and Fragmentation

	Intra-Individual Variability in Sleep Duration		Intra-Individual Variability in Sleep Fragmentation	
	β^*	<i>p</i>	β^{**}	<i>p</i>
Stressful Life Events	.19	.02	.15	.03
Negative Affect	.001	.98	.03	.70
Norepinephrine	.06	.48	.15	.03
Stressful Events X Negative Affect	-.03	.72	.19	.006
Norepinephrine x Negative Affect	.15	.04	.16	.01

* adjusted for age, sex, race, BMI, apnea-hypopnea index, and mean sleep duration.

** adjusted for age, sex, race, BMI, apnea-hypopnea index, and mean sleep fragmentation.

Note. The analyses were conducted separately for stressful life events and norepinephrine as main effects. Interactions were tested with the appropriate main effects and interaction term in the model.