Nonrestorative sleep in healthy, young adults without insomnia: associations with executive functioning, fatigue, and pre-sleep arousal

Ruben Tinajero, MS a,⁎, Paula G. Williams, PhD a, Matthew R. Cribbet, PhD b, Holly K. Rau, PhD c, Daniel L. Bride, MS a, Yana Suchy, PhD a

a University of Utah
b Texas Tech University
c Puget Sound VA

ARTICLE INFO

Article history:
Received 24 September 2017
Received in revised form 9 February 2018
Accepted 19 February 2018

ABSTRACT

Objectives: Previous research suggests that nonrestorative sleep (NRS), even in the absence of insomnia symptoms or other sleep disorders, may be associated with daytime dysfunction. This study examined the association between NRS and daytime dysfunction in healthy adults screened for insomnia and sleep apnea.

Design: Multi-day assessment approach.

Setting: Community-based adults and college students.

Participants: Healthy young adults without insomnia and sleep apnea (n = 79; 68% female, mean age = 27.5, SD = 6.5).

Measurements: Laboratory protocol included a behavioral assessment of executive functioning (EF), self-report of prior month sleep-related daytime dysfunction, and depressive symptoms in the prior two weeks. Subsequently, participants completed an experience sampling assessment that included morning ratings of NRS, repeat affect ratings throughout the day via palm-pilot, nighttime ratings of pre-sleep arousal and EF disturbances, ambulatory cardiac impedance monitoring, and wrist actigraphy.

Results: NRS was significantly associated with poorer performance on behaviorally-assessed EF, perceived EF difficulties, daily ratings of fatigue, and past-month reported daytime dysfunction. These associations remained significant after controlling for age and sleep duration (measured by actigraphy). NRS was also associated with increased sympathetic nervous system activation prior to bedtime. Further, reported pre-sleep arousal was associated with NRS, and this association was mediated by perceived EF difficulties.

Conclusions: Findings indicate that, even among healthy, young adults without insomnia or sleep apnea, NRS is associated with poorer cognitive functioning and may be a precursor to insomnia.

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Epidemiological studies indicate that insomnia is prevalent in the general population; approximately one third of adults report at least one insomnia symptom. Prior research on insomnia symptoms has focused predominantly on nocturnal symptoms, including difficulties initiating sleep and difficulties maintaining sleep. These symptoms, along with perceived poor quality sleep, are central to the conceptualization and diagnosis of insomnia. Nonrestorative sleep (NRS), sometimes considered a core symptom of insomnia, has recently received more attention in sleep research. NRS refers to the subjective experience of feeling unrefreshed upon awakening that is not attributed to lack of sleep. NRS is a characteristic complaint in patients with chronic fatigue syndrome, fibromyalgia, and organic sleep disorders such as sleep apnea. Past research also indicates that NRS is common in the general population and is associated with significant impairment. Compared to individuals who reported difficulties initiating or maintaining sleep (without NRS), individuals with NRS report more daytime dysfunction. Furthermore, recent research indicates that NRS is prospectively associated with the onset of a number of chronic diseases. Accordingly, additional research is needed to better understand the mechanisms and correlates of NRS to inform prevention and intervention efforts.

Importantly, NRS can occur in the absence of other insomnia symptoms. This is acknowledged in the DSM-5, as the presence of NRS without difficulties initiating or maintaining sleep and under conditions of conventional sleep duration is sufficient for the diagnosis of “other specified insomnia disorder”. Past research has demonstrated that “NRS-only” is related both concurrently and prospectively to psychopathology (e.g., anxiety and depressive disorders). Additionally, there is preliminary evidence that NRS-
only may be associated with daytime dysfunction, such as cognitive difficulties, fatigue, and mood disturbance. However, more research is needed to determine whether NRS-only is a construct that is distinct from insomnia in these associations. In particular, there is a need to better characterize the types of daytime dysfunction that are associated with NRS-only, as well as to examine whether known risk factors for insomnia are also associated with NRS-only. The goal of the present study was to investigate whether a broad range of both objective and subjective indices of daytime dysfunction are associated with NRS in individuals who do not have insomnia or sleep apnea, and whether NRS-only is associated with pre-sleep arousal, an established vulnerability factor for the development of insomnia.

Methodological issues in the study of Nonrestorative Sleep (NRS)

Epidemiological studies report a broad range of prevalence rates of NRS in the general population, ranging from 1.4 to 35%. This inconsistency is emblematic of a number of challenges faced by NRS researchers. First, within the sleep research literature, there is considerable heterogeneity in the conceptualization and operationalization of the NRS construct. This heterogeneity has made it difficult to draw definitive conclusions across studies regarding the prevalence, as well as the role NRS plays in sleep disorders and other health problems. In recent years, it has been suggested that the conceptualization of NRS should mirror the approach used for insomnia, such that NRS can be framed as both a consequence of medical or psychiatric conditions (though the underlying mechanisms are still largely unknown), as well as a stand-alone condition.

A second major challenge in the study of NRS involves assessment. A review by Vernon and colleagues highlighted the heterogeneity in the assessment of NRS. Additionally, there are currently no objective markers that reliably identify NRS. In the sole study that compared polysomnographic data between NRS-only participants and healthy controls, the only observed group differences were that NRS-only individuals exhibited less time in sleep stages 3 and 4 (specifically in the first hour of the night) and in REM sleep. Yet, these differences were minimal and would not reliably classify individuals into NRS and non-NRS categories. Regardless of potential objective markers, NRS is a perception and has necessarily relied on self-report. The recently published Restorative Sleep Questionnaire and the Nonrestorative Sleep Scale are two promising, validated questionnaires that may address some of the assessment challenges of NRS. Importantly, the timing of NRS assessment is variable across studies, with some using sleep diaries to obtain NRS ratings over multiple days and others using retrospective reports. Given the specific focus on feelings “upon awakening,” morning ratings should be the most accurate method of NRS assessment.

Lastly, it has also been suggested that the inclusion of NRS as a primary symptom of insomnia is problematic given that it is commonly associated with other conditions such as anxiety and depressive disorders, fibromyalgia, and chronic fatigue syndrome. Thus, additional research is needed to investigate the association between NRS and daytime dysfunction in individuals without such conditions.

NRS and daytime dysfunction

Historically, it was suggested that there is less daytime dysfunction in NRS-only compared to NRS with other insomnia symptoms. However, there is recent evidence that NRS-only is associated with significant daytime fatigue, sleepiness, and decreased work productivity. Furthermore, NRS-only is associated with self-reported cognitive and affective difficulties (depression, anxiety, irritability). Importantly, prior studies have largely relied on concurrent, retrospective, one-time assessments of NRS and daytime dysfunction. Consequently, these studies cannot determine whether NRS assessed upon awakening may set the stage for dysfunction later in the day.

Additionally, past research has often relied on single-item self-report assessments of daytime dysfunction. Such assessments may be limited by poor reliability and a lack of nuanced measurement of daily difficulties. Further, reliance on self-report makes it difficult to determine whether reporting biases could explain the observed associations between NRS and daytime dysfunction. This is particularly problematic for self-report of cognitive difficulties, as much research has shown that these reports are more strongly related to psychiatric symptoms (which are also presumably associated with NRS) than to objective cognitive performance. Although research has demonstrated that insomnia is related to poor performance on objective cognitive measures, most notably the cognitive domain known as executive functioning, the association between NRS and objective cognitive performance has yet to be investigated. Similarly, there is a need for research investigating the association between NRS and vulnerability factors related to the onset of sleep disturbance, such as pre-sleep arousal.

NRS and pre-sleep arousal

Prominent models for the development and maintenance of insomnia suggest that predisposing and precipitating factors lead to acute insomnia that may become chronic with the emergence of perpetuating factors. Specifically, hyperarousal (chronic psychological and physiological arousal) is believed to play a critical role in the development and maintenance of insomnia. In related research, Nozinger and colleagues found that pre-sleep cognitive arousal is a vulnerability factor for the development of insomnia. Indeed, Fernandez-Mendoza and colleagues found that in comparison to good sleepers, individuals with insomnia demonstrated higher global cerebral glucose metabolism when transitioning from awake to sleep states. Specifically, they found that prior to sleep, individuals with insomnia displayed a smaller metabolic decrease in brain regions that promote wakefulness, including the prefrontal regions of the brain implicated in executive functioning. Furthermore, individuals with insomnia demonstrated reduced pre-frontal cortex activation upon awakening. Thus, it was concluded that daytime fatigue experienced by individuals with insomnia may reflect reduced pre-frontal cortex activation. These findings have implications for the study of NRS. Perceptions of poor restoration upon awakening may reflect reduced pre-frontal cortex activation, suggesting a shared mechanism with pre-sleep arousal. Thus, examination of NRS associations with pre-sleep arousal is a logical next step. Further, it is possible that daytime dysfunction may mediate the association between NRS and pre-sleep arousal. This would suggest a reciprocal, feed-forward cycle of NRS leading to daytime dysfunction, which in turn sets the stage for pre-sleep arousal and further vulnerability to nonrestorative sleep. The current study sought to examine NRS-pre-sleep arousal associations, as well as hypothesized mediation pathways.

Current study

In summary, past research shows that (a) self-reported NRS-only is associated with a concurrent self-report of daytime dysfunction, including self-reported cognitive and emotional difficulties and fatigue, and (b) insomnia is related to high pre-sleep arousal. However, it is not known whether self-reported NRS upon awakening, in the absence of insomnia and sleep apnea, predicts (a) self-reported daytime dysfunction assessed later in the day, (b) objectively-assessed cognitive functioning, and (c) pre-sleep cognitive and somatic arousal.
The purpose of the present study was to address the gaps in the literature by examining the association between NRS-only and (a) daytime dysfunction (cognitive functioning, daily affect, and fatigue ratings) and (b) pre-sleep arousal in a sample of healthy, young adults screened for insomnia and sleep apnea. To these ends, participants completed laboratory assessments that included behavioral executive functioning assessment, self-reported past month sleep disturbance, depressive symptoms in the past two weeks. A multi-day assessment included morning NRS ratings, as well as nighttime ratings of pre-sleep arousal and perceived difficulties with executive functioning each day. In addition, a full day of experience-sampled affect ratings, including fatigue, were obtained. It was hypothesized that greater NRS would be associated with greater daytime dysfunction, including (a) past-month ratings of sleep-related daytime dysfunction, (b) greater negative valence/low arousal affect and higher fatigue ratings, (c) poorer behaviorally-assessed executive functioning. It was also hypothesized that NRS would be associated with higher reported pre-sleep arousal, as well as daytime sympathetic nervous system activity, quantified as pre-ejection period (PEP) assessed with ambulatory impedance cardiography. Lastly, we hypothesized that the association with pre-sleep arousal would be mediated by daytime dysfunction.

Methods

Participants

Participants were 79 healthy, young adults (32% male; mean age = 27 years, SD = 6.5, Age range = 20-45 years-old) recruited from the University of Utah participant pool and the greater Salt Lake City community. The racial composition was 91% Caucasian, 5% Asian Pacific, and 4% unspecified. Careful screening was done to ensure that the final sample was healthy and did not have insomnia or sleep apnea. Exclusionary criteria included primary language other than English; age beyond 20-45 years (to rule out age-related cognitive changes); and reported clinical insomnia symptoms (Insomnia Severity Index total cut-off score of 14). Absence of insomnia in the recruited sample was supported by an ISI sample average of 5 (SD = 3.8). Additional exclusionary criteria included: left hand dominance (because of differing cognitive profiles compared to right-handers); motor or sensory impairments that could interfere with cognitive task performance (e.g., uncured visual or hearing limitations, paralysis or tremor in the right hand, etc.); current use of tobacco; current pregnancy; history of renal failure, pulmonary disorder, hypertension, major orthopedic surgery, Multiple Sclerosis, heart surgery, brain surgery, brain tumor, cerebral vascular accident, seizures, and brain injury; and current use of neuroleptic, cardiovascular, or hypnotic medications. Exclusion of obstructive sleep apnea was based on screening for prior diagnosis of pulmonary disorder. Additionally, the Pittsburgh Sleep Quality Index (PSQI) item 5e was examined in the final sample: “During the past month, how often have you had trouble sleeping because you cough or snore loudly,” rated on a scale of 0 (not during the past month) to 3 (three or more times a week); the item average was .19 (SD = .51). Additionally, the mean body mass index calculated based on self-reported height and weight was 26.1 (SD = 5.5).

Procedures

The study was approved by the University of Utah Institutional Review Board (IRB). Participants were recruited using IRB-approved flyers posted at the University of Utah campus and in the Salt Lake City community. Participants were also recruited from the University of Utah Psychology Department participant pool. A trained research assistant contacted prospective participants to conduct a structured interview by phone to screen for the exclusionary criteria described above. Participants who qualified for the study completed a laboratory assessment that included standardized behavioral testing of EF, self-reported sleep disturbances in the previous month, and depressive symptoms in the prior two weeks. Subsequently, participants completed a 3-day experience sampling assessment that included: 1) morning ratings of NRS (3 days); 2) repeat affect ratings throughout the day via palm-pilot (1 day); 3) nighttime ratings of pre-sleep arousal and EF disturbances (2 nights); 4) ambulatory cardiac impedance monitoring (1 day; continuous); and 5) wrist actigraphy (3 days). Participants received a telephone call or text message (depending on their preference) each night they were part of the study to remind them to complete the nighttime inventories and the sleep diary upon awakening.

Measures-laboratory baseline

Pittsburgh Sleep Quality Index (PSQI)

The PSQI is a self-report measure that assesses sleep quality and disturbances during the previous month. The scale consists of 19 items which are used to derive seven component scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. The item-level daytime dysfunction subscale was the primary focus of the current study. Previous research indicates that this is the component of the PSQI significantly positively associated with the Epworth Sleepiness Scale. In the current study, Cronbach’s alpha for the PSQI global score was .71 and .65 for the daytime dysfunction subscale.

Beck Depression Inventory-II (BDI-II)

Participants completed the BDI-II, a well-validated self-report inventory of depressive symptoms experienced over the past two weeks. It consists of 21 items, on a scale from 0 to 3, with higher scores indicating greater depression severity. The total BDI-II score was used in analyses. In this study, Cronbach’s alpha for the BDI-II was .89.

Delis-Kaplan Executive Function System (D-KEFS)

As we have done in our prior work on executive functioning, we administered four subtests from the D-KEFS, from which 8 scores reflecting central aspects of executive functions (EF) were used to create an EF composite: Trail Making (Letter Number Sequencing completion time), Verbal Fluency (Letter and Category Fluency, number of correct words), Design Fluency (number of correct designs for each of the three conditions), and Color-Word Interference (Inhibition and Inhibition/Switching completion times). A composite score was created by averaging across the 8 age-corrected scaled scores (per test manual). Overall, performance on the 4 subtests relies on working memory and generative fluency, mental flexibility, set-maintenance, inhibition, initiation, and response selection (chapter 8).

Importantly, cognitive functions are organized hierarchically, with higher-order processes like EF relying on lower-order processes. To control for non-EF aspects of test performance, we also created a composite of lower-order processes by averaging the age-corrected scaled scores of six conditions including Color Naming and Word Reading from the Color-Word Interference Test, and Visual Scanning, Number Sequencing, Letter Sequencing, and Motor Speed from the Trail Making Test. Next, we controlled for the lower-order processes by removing their variance from the EF composite, resulting in an unstandardized residual of the EF composite, reflecting EF without confounding lower-order processes. The unstandardized residual of the EF composite was used in all subsequent analyses.
Due to procedural modifications early in the study, 12 participants received all of the DKEFS measures except for the Trail Making Test. We therefore imputed the missing values using scores obtained from the nine other test conditions that were included in the executive and nonexecutive composites, together with demographic variables (i.e. age, education, and gender), to predict the missing values. Cronbach’s alphas were .75 for the executive composite and .81 for the nonexecutive composite.

Measures-experience sampling and ambulatory Nonrestorative sleep
As part of a morning sleep diary, participants were asked to answer an item from a validated sleep diary56: How rested or refreshed did you feel this morning? for each of three days. The item was rated on a 4-point Likert scale ranging from 0 (very much rested/refreshed) to 4 (not at all), with higher ratings indicating more nonrestorative sleep. Similar items also appear on other validated sleep diaries, such as the Consensus Sleep Diary.57 An average of the three morning ratings was used for subsequent analyses. Cronbach’s alpha for NRS was .59.

Perceived EF difficulties
At the end of each assessment day, participants were asked to complete a questionnaire assessing difficulties in executive functioning experienced throughout that day. Nine representative items, rated on a five-point Likert scale ranging from 0 (not at all) to 4 (constantly), were selected from the Behavior Rating Inventory of Executive Function58 and the Conners’ Adult ADHD Rating Scales.59 These items were used to assess subjective difficulties in the following domains, each with the qualifier “Thinking about today only . . .”: 1) emotion regulation (“To what extent did you get upset or angered over little things”; “To what extent did you react more emotionally to situations than you usually do”; “To what extent did you feel easily frustrated”); 2) behavioral regulation (e.g. “To what extent did you say or do things without thinking”; “To what extent did you interrupt other people more than usual”; “To what extent did you feel easily frustrated”); and 3) cognitive difficulties (e.g. “To what extent did you have difficulty concentrating on or completing tasks”; “To what extent did you have difficulty thinking things through before acting”; “To what extent did you forget what you were doing or saying in the middle of things”). Perceived difficulties in EF across both days were averaged and used in the analyses. Cronbach’s alphas for average scores were .83 for total perceived EF difficulties, .76 for emotion regulation, .78 for cognitive difficulties, and .63 for behavioral regulation.

Affect ratings
Sixteen emotion descriptors were used from the affective circumplex,60 including positive valence/high arousal (i.e., excited, elated, alert, happy), positive valence/low arousal (i.e., relaxed, calm, serene, contented), negative valence/high arousal (i.e., stressed, tense, upset, nervous), and negative valence/low arousal (i.e., sad, lethargic, depressed, fatigued). Each affect rating contained the same stem question (e.g. “How _____ do you feel right now?”) and was rated on a five-point Likert scale from 1 (not at all) to 5 (very much). Participants received a total of 14 prompts throughout the day. The order of the affect items was randomized for each prompt in order to reduce overlearned and careless responding. An average score for each of the 16 affect ratings was calculated. Average score ratings for each affect item were then used to calculate summary scores for positive valence/high arousal, positive valence/low arousal, negative valence/high arousal, and negative valence/low arousal scores. Cronbach’s alphas for the affective summary scores were .57 for positive valence/high arousal, .81 for positive valence/low arousal, .94 for negative valence/high arousal, and .89 for negative valence/low arousal. Given prior associations between NRS and fatigue, the average rating for this item was also examined separately.

Pre-sleep arousal scale41
Participants rated levels of cognitive and somatic pre-sleep arousal before going to bed each night. The PSAS is a self-report measure comprised of 16 items rated from 1 (not at all) to 5 (extremely) that assess cognitive (e.g., worry related to sleep, inability to shut off thoughts, depressing or anxious thoughts) and somatic (e.g. upset stomach, racing heart, shortness of breath) arousal states at bedtime. A total score was obtained by summing all items, with higher scores indicating greater pre-sleep arousal. Higher scores on the PSAS reliably differentiate between normal sleepers and patients with clinical insomnia.42 Average of PSAS scores were calculated and used in the analyses. Cronbach’s alphas for were .89 for the total score, .88 for the cognitive arousal subscale, and .71 for the somatic arousal subscale.

Sympathetic nervous system arousal - Pre-ejection Period (PEP)
Participants wore an ambulatory physiology monitor continuously for 1 day (MW1000A ambulatory heart rate variability and impedance cardiography monitor; Mindware Technologies; Gahanna, Ohio). A combination of self-reported sleep onset and actigraphy were used to determine the 30-minute time period prior to sleep onset to be used for psychophysiological data reduction. ECG data were collected from participants using three spot electrodes placed in the standard lead II configuration. The ECG was measured continuously at a sampling rate of 500Hz. Four spot electrodes were placed according to guidelines for impedance cardiography.61 One spot electrode was placed at the base of the neck, one at the xiphisternal junction, one over the fourth cervical vertebra, and one over the ninth thoracic vertebra. The impedance signal (Zo) and the derivative (dZ/dt) signals were digitized at 500 Hz. The raw ECG data was initially inspected by automated software and subsequently visually inspected according to established guidelines.62,63 ECG complexes were ensemble averaged for each minute. Ensemble averaging uses the R-point of the ECG as a reference for the successive averaging of the ECG and subsequent dZ/dt signals. PEP was calculated as the time interval in ms between the Q-point of the ECG and the B-point and X-point of the dZ/dt signal. Each minute was used to compute an average PEP score that reflected sympathetic activation for the 30 minutes prior to sleep onset. PEP average scores were available for 41 participants. Analysis of variance showed that there were no mean differences in NRS between participants with and without F (1,69) = 0, p > 0.05.

Actigraphy
Participants wore actigraphs (Actigraph GT1M, The Actigraph, Pensacola, Florida) on their non-dominant wrists continuously for three days. Actigraphs were programmed to collect rest and activity data in 60 second epochs. Each actigraphy study was evaluated by a scorer who used a standardized approach to set rest intervals (periods when the participant was trying to sleep) based on input from sleep diaries. For each day, a primary rest interval was identified as the primary period for sleep based on information from the sleep diary. Once rest intervals were set, a medium-sensitivity scoring algorithm64 from the Actiware 5 software was used to distinguish sleep onset and sleep offset and a wake threshold activity count of 1000 was applied to generate sleep/wake from each epoch. The actigraphic variable of interest was total sleep time on each of the 3 nights. A total sleep time average score across the 3 days was calculated and used in the analyses.
Statistical approach

Hypothesized associations were examined initially with zero-order correlations. To examine the relationship between NRS and daytime dysfunction, behavioral assessment of EF, reported difficulties in EF, daily ratings of fatigue, and prior-month sleep related dysfunction were regressed onto NRS in separate regression models, controlling for age and actigraphy-determined sleep duration. Mediation analysis investigated the indirect effect of daytime dysfunction factors on the relationship between NRS and pre-sleep arousal. All analyses were conducted using IBM SPSS Statistics for Windows Version 25 and bootstrapping mediation analyses were conducted using PROCESS.66

Results

Zero order correlations and descriptive statistics

Zero-order correlations and descriptive statistics are presented in Table 1. Results indicated that NRS was negatively associated with performance on the behavioral measure of EF (D-KEFS), positively associated with reported EF, past month sleep related daytime dysfunction, and daily ratings of fatigue, but was not significantly associated with other affect ratings, including negative valence/low arousal affective ratings. Additionally, NRS was positively associated with reported pre-sleep arousal and depressive symptoms.

Regression analyses

Separate regression analyses were used to examine the association between NRS (predictor) and performance on the behavioral measure of EF, perceived EF difficulties, fatigue, and past-month sleep related daytime dysfunction (dependent variables in separate analyses), controlling for age and actigraphy-measured sleep duration. As presented in Table 2, NRS remained significantly associated with each of these daytime dysfunction measures. Results indicated that NRS was negatively associated with behaviorally-assessed EF and positively associated with perceived difficulties in EF, fatigue, and past-month sleep related daytime dysfunction.

Next, the association between NRS and reported pre-sleep arousal and sympathetic activation prior to sleep onset was further examined. As presented in Table 1, NRS was significantly associated with reported pre-sleep arousal. Subscale analyses indicated that NRS was positively associated with both pre-sleep cognitive (B = 0.58, β = 0.24, p < 0.05) and somatic (B = 1.42, β = 0.27, p < 0.05) arousal. In a regression model controlling for age and sleep duration, NRS remained significantly associated with pre-sleep arousal (B = 2.6, β = 0.35, p < 0.05) whereas sleep duration (B = -.01, β = -0.09, p > 0.05) and age (B = 0.04, β = 0.05, p > 0.05) were not significantly associated. In addition, NRS was significantly associated with sympathetic nervous system activation before sleep, quantified as average PEP in the 30 minutes before sleep onset, (B = -8.1, β = -0.33, p < 0.05), with shorter PEP indicating greater sympathetic activity. In a regression model controlling for age and sleep duration, NRS remained significantly associated with PEP (B = -9.4, β = -0.36, p < 0.05). Age (B = -0.15, β = -0.05, p > 0.05) and sleep duration (B = -0.05, β = -0.18, p > 0.05) were not significantly associated.

Mediation analyses

In order to assess the hypothesized indirect effect of NRS on pre-sleep arousal through daytime dysfunction, PROCESS for SPSS66 was used to conduct bootstrapping mediation analyses. Specifically, 5000 samples were drawn using bootstrapping procedures to calculate bias corrected bootstrap confidence intervals. The pattern of correlations suggested that, of the daytime dysfunction measures,

Table 1
Zero-order correlations among study variables

<table>
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<th>1</th>
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<td>3. Perceived EF Difficulties</td>
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<td>4. Fatigue</td>
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<td>5. PSQI-Daytime Dysfunction</td>
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<td>-0.07</td>
<td>0.32</td>
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<td>6. Positive Valence / High Arousal</td>
<td>-0.24</td>
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<td>0.08</td>
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<td>8. Negative Valence / High Arousal</td>
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<td>9. Pre-Sleep Arousal</td>
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<td>10. Depression</td>
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Note: Correlations in boldface indicate p < 0.05. NRS—nonrestorative sleep; Behavioral EF—D-KEFS unstandardized residual; Perceived EF Difficulties-reported difficulties in EF experienced throughout the day; Fatigue-average ratings of fatigue; PSQI-Daytime Dysfunction-average of items 8 and 9 from the PSQI; Positive Valence / High Arousal- average from excited, elated, alert, happy emotion descriptors; Positive Valence / Low Arousal- average from relaxed, calm, serene, contended affective descriptors; Negative Valence / High Arousal- average of stressed, tense, upset, nervous emotion descriptors; Pre-Sleep Arousal- average PSAS score; Depression-BDI total score; Sleep Duration-average of 3 days measured by actigraphy.

Table 2
Associations between NRS and daytime dysfunction, controlling for age and sleep duration (actigraphy)

<table>
<thead>
<tr>
<th></th>
<th>β</th>
<th>t</th>
<th>p</th>
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<tr>
<td>DV: Behavioral Measure of EF</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>.02</td>
<td>.14</td>
<td>&gt;.05</td>
<td></td>
</tr>
<tr>
<td>Sleep Duration</td>
<td>.09</td>
<td>.71</td>
<td>&gt;.05</td>
<td></td>
</tr>
<tr>
<td>NRS</td>
<td>-.29</td>
<td>-2.3</td>
<td>.02</td>
<td>.08</td>
</tr>
<tr>
<td>Total R² = .09</td>
<td></td>
<td></td>
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<tr>
<td>DV: Perceived EF Difficulties</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>.01</td>
<td>.08</td>
<td>&gt;.05</td>
<td></td>
</tr>
<tr>
<td>Sleep Duration</td>
<td>.03</td>
<td>.2</td>
<td>&gt;.05</td>
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<tr>
<td>NRS</td>
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<td>.12</td>
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<tr>
<td>Total R² = .13</td>
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<tr>
<td>DV: Fatigue</td>
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<tr>
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<td>.5</td>
<td>&gt;.05</td>
<td></td>
</tr>
<tr>
<td>Sleep Duration</td>
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<td>1.8</td>
<td>&gt;.05</td>
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<tr>
<td>NRS</td>
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<td>.00</td>
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<td>Total R² = .26</td>
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<td>DV: PSQI-Sleep Related Daytime Dysfunction</td>
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<td></td>
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<tr>
<td>Age</td>
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<td>-1.1</td>
<td>&gt;.05</td>
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<tr>
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<td>Total R² = .09</td>
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Notes: NRS—nonrestorative sleep; Behavioral Measure of EF—D-KEFS unstandardized residual; Perceived EF Difficulties-reported difficulties in EF experienced throughout the day; Fatigue-average ratings of fatigue; PSQI-Sleep Related Daytime Dysfunction-average of items 8 and 9 from the PSQI.
perceived EF difficulties may mediate the association between NRS and pre-sleep arousal. As reported in Table 1, NRS, daily EF ratings, and pre-sleep arousal were inter-correlated. Results indicated a significant indirect effect of NRS on pre-sleep arousal through perceived difficulties in EF ($b = 1.28$, 95% CI [0.5, 2.6]). The direct effect of NRS on pre-sleep arousal was not significant ($b = 1.34$, 95% CI [-3, 2.97]). The results were thus indicative of full mediation. This pattern of findings remained significant after controlling for sleep duration.

Although this was the hypothesized pattern of mediation, based on the prior literature, the concurrent nature of the data means that other mediation paths are also plausible. One alternate mediation model would involve NRS as a mediator of the relationship between pre-sleep arousal and difficulties in EF. To examine the specificity of the reported model, this alternative model was also tested. Bootstrapping mediation analysis indicated that the indirect effect of pre-sleep arousal on reported difficulties in EF through NRS was significant ($b = 0.04$, 95% CI [0.00, 0.12]). The direct effect of pre-sleep arousal on difficulties in EF was also significant ($b = 0.31$, 95% CI [1.6, 45]). Thus, the results were indicative of partial mediation. Overall, the pattern of mediation analyses most strongly supports the hypothesized mediational path from NRS to pre-sleep arousal via daytime cognitive functioning. Importantly however, there are likely reciprocal associations over time, supported by the effects seen in the alternate model.

Discussion

The current study examined the association between NRS and daytime dysfunction in healthy, young adults without insomnia or sleep apnea. Results indicated that NRS is broadly associated with both objective and perceived daytime dysfunction, including poorer cognitive performance in addition to perceived difficulties in EF. Further, these associations between NRS and EF remained significant after controlling for age and average actigraphy-determined sleep duration. This study is the first to demonstrate that morning ratings of poor restoration from sleep are associated with objective cognitive performance in addition to perceived difficulties in daily life. These findings support the notion that NRS, in the absence of insomnia or sleep apnea, is associated with objective daytime functioning. Additional research is needed to investigate mechanisms for these associations. For example, monitoring for sleep-related threat cues, such as physical/bodily signs of fatigue, is a potential mechanism linking morning perception of NRS and subsequent daytime dysfunction. Monitoring for sleep-related threat cues increases subsequent negative thoughts related to poor sleep and thus may also play an important role in the experience of NRS over time. Such attentional focus on bodily signs of poor sleep is also likely implicated in conditions such as fibromyalgia and chronic fatigue syndrome. Interestingly, other studies have demonstrated that EF is subject to depletion as a result of increased emotion regulation demands. Importantly, such demands may themselves be associated with poor sleep quality, which points to the complexity and multivariate nature of potential explanations for this effect. Biological mechanisms including inflammation should also be further explored.

NRS was also associated with past-month ratings of sleep-related daytime dysfunction. This finding is consistent with previous studies that showed an association between NRS and reported daytime dysfunction in populations without insomnia. In addition, NRS was positively associated with daily ratings of fatigue. This finding replicated previous research that showed an association between NRS and fatigue in populations without insomnia symptoms. Contrary to prediction, NRS was not strongly associated with other negative valence/low arousal affect ratings. It should be noted that although it did not reach statistical significance in the current sample, there did appear to be a modest negative association with high-arousal positive affect ratings. Should this be replicated in future research, it would suggest a potential mechanism for NRS associations with depressed mood over time. Overall, these findings confirm the centrality of fatigue as a daytime consequence of NRS, particularly among healthy individuals who do not yet have significant sleep or mood disturbance.

NRS and daytime dysfunction

Prior studies have found that NRS is associated with reported cognitive difficulties, though the association has often been with single-item concurrent measures. In the current study, NRS was associated with both perceived daily EF difficulties and performance on a behavioral measure of EF. Further, these associations between NRS and EF remained significant after controlling for age and average actigraphy-determined sleep duration. This study is the first to demonstrate that morning ratings of poor restoration from sleep are associated with objective cognitive performance in addition to perceived difficulties in daily life. These findings support the notion that NRS, in the absence of insomnia or sleep apnea, is associated with objective daytime functioning. Additional research is needed to investigate mechanisms for these associations. For example, monitoring for sleep-related threat cues, such as physical/bodily signs of fatigue, found that parents who are vulnerable to stress-related insomnia have offspring that demonstrated cognitive-emotional arousal and poor coping skills. Accordingly, future research should investigate stress regulation factors such as exposure to stressors (e.g., daily hassles) and prolonged reactivity to stress as potential mediators of the relationship between NRS and pre-sleep arousal. The current study highlights the existence of multiple vulnerability factors for pre-
sleep arousal among healthy, young adults that have not developed insomnia or other sleep problems. Accordingly, it may be beneficial to include assessments of sleep restoration, mood, and cognitive difficulties as potential targets for pre-sleep arousal prevention.

Findings from the current study indicated that NRS is associated with depressive symptoms amongst individuals without insomnia or sleep apnea, consistent with prior research.\textsuperscript{8,9,11} Future research should seek to clarify how NRS and mental health problems influence one another longitudinally and whether treating one may mitigate the other.\textsuperscript{4} In addition, the current study found that NRS was not associated with actigraphy-assessed sleep duration. Ohayon\textsuperscript{6} found that shorter sleep duration was associated with a higher prevalence of NRS. However, results from a multivariate model suggested that shorter sleep duration was a protective factor for NRS and that sleep duration over 9 hours was a risk factor for NRS. Ohayon\textsuperscript{8} concluded that the relationship between short sleep duration and NRS was explained by other factors.

Limitations and future directions

Strengths of the current study include morning assessment of NRS across multiple days, the use of a well-validated behavioral assessment of EF, experience-sampling assessment of affect including fatigue, use of actigraphy to assess sleep duration, subjective and objective indices of pre-sleep arousal, and screening for insomnia and sleep apnea that permitted investigation of “pure” NRS in a healthy sample. Despite these strengths, several limitations should be considered. The restricted age range in the current study was implemented in order to limit the effects of aging on cognitive performance (i.e. behavioral assessment of EF). Nevertheless, generalization should be made cautiously as controlling for age in a restricted age range sample is of limited utility. Additional research is needed to investigate the relationship between NRS “only” and daytime dysfunction across the adult lifespan.

Although the current study was adequately powered for the statistical tests utilized (including bootstrapping mediation), the relatively modest sample size is acknowledged. It is possible that there are small effects, particularly of experience-sampled affect, that were not detected. Larger scale ESM studies would be useful in examining more nuanced associations with daily affect. In addition, the current study used a single item to assess NRS. Obtaining NRS morning ratings over multiple days is consistent with prior sleep diary research; however, the findings of this study should be replicated and extended with recently published measures of NRC\textsuperscript{30,31} preferably collected upon awakening. It should also be noted that only a subset of the sample had viable PEP data available for analyses, thus the association between NRS and pre-sleep sympathetic nervous system activation should be replicated in larger samples. It is also the case that definitive demonstration of successful screening for sleep apnea would require overnight polysomnography. Although it is unlikely that there was undiagnosed sleep apnea in this young, healthy sample, the lack of an apnea-specific specifier, such as the STOP-bang sleep apnea questionnaire\textsuperscript{72,73} is a limitation. Additionally, associations among NRS, daytime dysfunction, and pre-sleep arousal are based on summary scores across days, precluding the ability to make strong inferences about causal direction. This limitation is especially relevant for the mediation analyses, given the concurrent nature of the data. Furthermore, Stone and colleagues\textsuperscript{4} recommended that individuals should be characterized as having NRS-only if reported three times per week for a month. Although these recommendations have been deemed arbitrary by other researchers,\textsuperscript{10} it is the case that the current study offers only a “snapshot” of NRS and daytime dysfunction correlates in daily life.

The findings of the current study provide support for the notion that NRS is associated with daytime dysfunction in the absence of insomnia or sleep apnea. The conceptualization of NRS is in its early stages and additional research is needed to understand biological mechanisms that account for the associations between NRS and mental and physical health problems (e.g., inflammation\textsuperscript{15}). Wilkinson and Shapiro\textsuperscript{10} suggested that the conceptualization of NRS should expand such that it be considered both a symptom with multiple causes, as well as a distinct condition. Whether or not this approach becomes standard practice, it is clear that even without the concomitant effects of other insomnia symptoms or sleep apnea, NRS is negatively associated with cognitive functioning and may represent a vulnerability factor for the development of chronic sleep disturbance, mood disturbance, and adverse health outcomes.

Disclosure

The authors have nothing to disclose.

Acknowledgments

This study was funded by a Funding Incentive Seed Grant from the University of Utah, the Mind and Life Institute, and Division 38 of the American Psychological Association.

References


