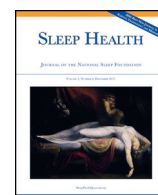




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Nonrestorative sleep in healthy, young adults without insomnia: associations with executive functioning, fatigue, and pre-sleep arousal

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

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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 population¹; approximately one third of adults report at least one insomnia symptom.^{2,3} Prior research on insomnia symptoms has focused predominantly on nocturnal symptoms, including difficulties initiating sleep and difficulties maintaining sleep.⁴ 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,⁵ 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.⁴ NRS is a characteristic complaint in patients with chronic fatigue syndrome, fibromyalgia, and organic sleep disorders such as sleep apnea.^{6,7} 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.⁸ Furthermore, recent research indicates that NRS is prospectively associated with the onset of a number of chronic diseases.⁹ 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.^{4,10,11} This is acknowledged in the DSM-5,¹² 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).^{8,13,9} Additionally, there is preliminary evidence that NRS-

* Corresponding author.

E-mail address: ruben.tinajero@psych.utah.edu (R. Tinajero).

only may be associated with daytime dysfunction, such as cognitive difficulties, fatigue, and mood disturbance.^{9,11,14,15} However, more research is needed to determine whether NRS-only is a construct that is distinct from insomnia in these associations.^{4,10} 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.^{16–18}

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%.^{8,13,19–29} 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.⁴ 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.¹⁰

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.⁵ Additionally, there are currently no objective markers that reliably identify NRS.⁴ 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.¹⁴ 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 Questionnaire³⁰ and the Nonrestorative Sleep Scale³¹ 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.⁴ 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.¹³ However, there is recent evidence that NRS-only is associated with significant daytime fatigue, sleepiness, and decreased work productivity.^{8,14} Furthermore, NRS-only is associated with self-reported cognitive^{11,32} and affective difficulties (depression, anxiety, irritability).³² 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 difficulties. 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.^{33,34} Although research has demonstrated that insomnia is related to poor performance on objective cognitive measures, most notably the cognitive domain known as executive functioning,³⁵ 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.^{36,37} Specifically, hyperarousal (chronic psychological and physiological arousal) is believed to play a critical role in the development and maintenance of insomnia.^{16,17,38} In addition, cognitive arousal prior to bedtime is common among people with insomnia.^{39–43} Indeed, Fernandez-Mendoza and colleagues¹⁸ found that pre-sleep cognitive arousal is a vulnerability factor for the development of insomnia. In related research, Nofzinger and colleagues⁴⁴ 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-report of 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.

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