Sleep Health 1 (2015) 249–256

Contents lists available at ScienceDirect

Sleep Health

Journal of the National Sleep Foundation

journal homepage: http://www.elsevier.com/locate/sleh

Sleep restriction and delayed sleep associate with psychological health and biomarkers of stress and inflammation in women

Jaime L. Tartar, PhD [a,*], Ana I. Fins, PhD [a], Andrea Lopez, MS [a], Linett A. Sierra, MS [a], Sarah A. Silverman, MS [a], Samuel V. Thomas, BS [a], Travis J.A. Craddock, PhD [a,b,c,d]

[a] College of Psychology, Nova Southeastern University, Ft Lauderdale, FL, USA
[b] College of Osteopathic Medicine, Nova Southeastern University, Ft Lauderdale, FL, USA
[c] College of Engineering and Computing, Nova Southeastern University, Ft Lauderdale, FL, USA
[d] Institute for Neuro-Immune Medicine, Nova Southeastern University, Ft Lauderdale, FL, USA

ARTICLE INFO

Article history:
Received 19 May 2015
Received in revised form 16 September 2015
Accepted 17 September 2015

Keywords:
Cortisol
Health
Inflammation
Melatonin
Mood
Sleep restriction
Women

ABSTRACT

Study objectives: Despite strong associations between sleep duration and health, there is no clear understanding of how volitional chronic sleep restriction (CSR) alters the physiological processes that lead to poor health in women. We focused on biochemical and psychological factors that previous research suggests are essential to uncovering the role of sleep in health.
Design: Cross-sectional study.
Setting: University-based.
Participants: Sixty female participants (mean age, 19.3; SD, 2.1 years).
Measurements: We analyzed the association between self-reported volitional CSR and time to go to sleep on a series of sleep and psychological health measures as well as biomarkers of immune functioning/inflammation (interleukin [IL]-1β), stress (cortisol), and sleep regulation (melatonin).
Results: Across multiple measures, poor sleep was associated with decreased psychological health and a reduced perception of self-reported physical health. Volitional CSR was related to increased cortisol and increased IL-1β levels. We separately looked at individuals who experienced CSR with and without delayed sleep time and found that IL-1β levels were significantly elevated in CSR alone and in CSR combined with a late sleep time. Cortisol, however, was only elevated in those women who experienced CSR combined with a late sleep time. We did not observe any changes in melatonin across groups, and melatonin levels were not related to any sleep measures.
Conclusions: New to our study is the demonstration of how an increase in a proinflammatory process and an increase in hypothalamic-pituitary-adrenal axis activity both relate to volitional CSR, with and without a delayed sleep time. We further show how these mechanisms relate back to psychological and self-reported health in young adult women.

Introduction

A large and growing body of evidence shows that reduced sleep duration, or chronic sleep restriction (CSR), has profound deleterious effects on health and well-being and is associated with a 10%-12% increase in all-cause mortality.[1,2] Despite the strong associations between sleep duration and health, there is no clear understanding of the mechanisms through which CSR alters the physiological processes that lead to poor health. One likely reason for this is that the vast majority of studies that have examined the effects of sleep loss on health have used experimental acute total sleep deprivation. However, most people rarely experience total sleep deprivation but rather experience volitional CSR. In other words, people tend to purposefully restrict their sleep time on a regular basis to meet the demands of daily life rather than missing entire nights of sleep. Controlled laboratory studies of CSR have been restricted to a few days or a week at most because of the limitations associated with extended participant testing.[3] Accordingly, the overall goal of the present study was to use self-report sleep measures in an effort to capture those individuals who experience *volitional* ongoing reduced sleep duration and use this information to begin to connect likely biochemical and psychological factors that combine to create the adverse health effects associated with CSR. A secondary interest here was to look at a female-specific population because, relative to men, the effects of sleep debt accumulate more quickly in women,[4]

* Corresponding author at: Nova Southeastern University, College of Psychology, Department of Psychology and Neuroscience, 3301 College Ave, Ft Lauderdale, FL, 33314, USA.
E-mail address: tartar@nova.edu (J.L. Tartar).

http://dx.doi.org/10.1016/j.sleh.2015.09.007
2352-7218/

sleep complaints in women are particularly associated with impaired psychological functioning,[5] and women are at a higher risk than men for CSR-related mortality.[6]

One way that sleep loss is thought to affect health is through direct effects on immune function. Robust evidence supports a bidirectional relationship between sleep and immune processes. For example, immune and endocrine pathways exhibit a strong circadian profile that is primarily governed by feedback pathways through and within the diencephalon that are vulnerable to deviations from a normal sleep-wake cycle. Within this bidirectional sleep-immune relationship, proinflammatory cytokines are key mediators in sleep regulation, and extensive evidence implicates interleukin (IL)-1β in particular as a major somnogenic factor.[7,8] Interleukin-1β administration in human and nonhuman animals increases spontaneous sleep and fatigue.[9,10] Underscoring the bidirectional nature of sleep and cytokine activity, sleep loss can also upregulate circulating IL-1β[11] as well as brain IL-1β mRNA levels.[12] For these reasons, we targeted IL-1β as our measure of immune changes with CSR.

We also examined the extent to which volitional CSR is associated with cortisol because CSR can act as a chronic stressor, resulting in activation of the hypothalamic-pituitary-adrenal (HPA) axis–[13,14] glucocorticoids have even been proposed to be entraining signals for sleep-wake cycles.[15] In general, sleep processes are inextricably tied to HPA axis functioning and cortisol activity in particular. Sleep is initiated when cortisol levels are at their circadian nadir, and cortisol levels peak before wake (the cortisol awakening response) to assist in the sudden energy demands associated with waking.[16] These patterns are disturbed in people with sleep difficulties. For example, chronic insomnia is linked with elevated evening cortisol levels.[17] Experimental CSR also results in an elevation in evening cortisol levels.[13] As the primary end-product of HPA axis activation, cortisol levels rise in response to stress followed by a predictable return to baseline levels due to negative feedback regulation at multiple levels of the HPA axis. However, ongoing stress can cause the HPA axis to become dysregulated, leading to impairments in negative feedback processes and, as a consequence, unpredictable stress responsivity and chronically elevated levels of cortisol. This is a key factor in the sleep-immune relationship because circulating cortisol works to rein in the immune system and decreases IL-1β levels in a dose-dependent manner.[18]

In addition to the direct effects of CSR on immune and endocrine processes, and of key interest to our investigation, alterations to psychological health that occur as result of sleep loss can also create or exacerbate poor health. In particular, sleep loss is associated with impaired psychological health factors such as stress, depression, loneliness, poor decision making, and impaired coping skills.[19,20] These alterations in psychological processing can then lead to poor health outcomes indirectly through impairments in health decision making or directly through psychoneuroimmune pathways.[21,22] Sleep disturbances that occur with psychological impairments are also reported to be related to a shift in melatonin output. For example, major depression is associated with lower melatonin levels and delayed onset relative to time to fall asleep.[23] Furthermore, and of note to the present study, experimental CSR also results in a delay in melatonin onset,[24] and melatonin induces the secretion of IL-1β from human peripheral blood mononuclear cells.[25]

In the present study, we examined the relationship between biochemical and psychological factors that previous literature suggests might be essential to uncovering the role of sleep in health in young adult women. To that end, we analyzed the association between self-reported CSR (sleep restriction over the previous month) and a series of sleep and psychological health measures as well as biomarkers of immune functioning/inflammation (IL-1β), stress (cortisol), and circadian misalignment (melatonin). In addition to sleep duration as a measure of CSR, we were also interested in looking at the time that the participants typically fall asleep because IL-1β levels peak approximately 2.5 hours after sleep onset and are at their nadir in the morning.[26]

Materials and methods

Participants

A sample of 66 female participants between the ages of 18 and 25 years completed all of the tasks for this study. They were compensated with either research credit for an introductory psychology course or with a $10 gift card. Participants taking medications affecting sleep or immune function were excluded from further study, reducing the cohort to 60 participants (mean age = 19.3, SD = 2.1 years). Of the 60 participants, 52.8% were non-Hispanic white, 23.9% Hispanic white, 8.3% African American/black, 10% Asian, 1.7% American Indian or Native Alaskan, and 3.3% of other racial ancestry. Ethical approval was granted by the Nova Southeastern University Institutional Review Board, and written informed consent was provided by all of the participants. Five participants reported being on oral contraceptives, and no participants reported being pregnant or breastfeeding. There was not a significant difference in the biochemical results between those women who were on oral contraceptives and those women who were not.

Biomarkers

Saliva samples were run in duplicate and quantified via human enzyme immunoassay kits per the manufacturer's instructions (Salimetrics LLC, USA). The samples were immediately read in a BioTek ELx800 plate reader (BioTek Instruments, Inc, USA) at 450 nm with a correction at 630 nm. All samples were within the detection ranges indicated in the cortisol, IL-1β, and melatonin immunoassay kits. The variation of sample readings was within the expected limits; the highest interassay coefficient of variation was 8.7% and the highest intraassay coefficient of variation was 6.3%. Final concentrations for the biomarkers were generated by interpolation from the standard curve in μg/dL for cortisol and pg/mL for IL-1β and melatonin.

Psychological instruments: sleep behavior

Pittsburgh Sleep Quality Index

Sleep quality was measured using the self-rated Pittsburgh Sleep Quality Index (PSQI) questionnaire.[27] The PSQI is a 19-item instrument that yields 7 component scores in addition to a global score of sleep quality. With strong psychometric properties, the instrument is used widely. The instrument exhibits high internal consistency (Cronbach $\alpha = 0.83$), adequate test-retest reliability scores across the sleep-related components of the instrument for a nonclinical sample (from 0.44 to 0.70), and the ability to differentiate controls from sleep-disordered groups.[27] Our sleep duration and time to go to sleep measures were taken from fill-in-the-blank items in the PSQI and were based on behavior over the previous month. Use of the sleep duration item has been shown to be significantly correlated with actigraphy-derived estimates of total sleep time in younger adults.[28] In addition, this estimate is in line with 30 days as the established period for diagnoses of chronic sleep disorders.[29]

Epworth Sleepiness Scale

The Epworth Sleepiness Scale (ESS) was used to evaluate the degree of daytime sleepiness. The scale consists of 8 items that evaluate