Psychoneuroendocrinology 79 (2017) 1–8

Contents lists available at ScienceDirect

Psychoneuroendocrinology

journal homepage: www.elsevier.com/locate/psyneuen

Investigating the effect of acute sleep deprivation on hypothalamic-pituitary-adrenal-axis response to a psychosocial stressor

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ARTICLE INFO

Article history:
Received 8 August 2016
Received in revised form 23 January 2017
Accepted 25 January 2017

Keywords:
Sleep
Stress
HPA axis
Cortisol
Sleep deprivation
Gender

ABSTRACT

The hypothalamic-pituitary-adrenal (HPA) axis has been previously identified as one potential mechanism that may explain the link between sleep deprivation and negative health outcomes. However, few studies have examined the direct association between sleep deprivation and HPA-axis functioning, particularly in the context of stress. Therefore, the aim of the current study was to investigate the relationship between acute sleep deprivation and HPA-axis reactivity to a psychosocial stressor. Participants included 40 healthy, young adults between the ages of 18–29. The current protocol included spending two nights in the laboratory. After an adaptation night (night 1), participants were randomized into either a sleep deprivation condition (29 consecutive hours awake) or a control condition (night 2). Following the second night, all participants completed the Trier Social Stress Test (TSST). Salivary cortisol was collected before, during, and after the TSST. Results indicated that there were significant group differences in cortisol stress reactivity. Specifically, compared to participants in the control condition, participants in the sleep deprivation condition had greater baseline (i.e., pre-stress) cortisol, yet a blunted cortisol response to the TSST. Taken together, a combination of elevated baseline cortisol (and its subsequent effect on HPA-axis regulatory processes) and a relative 'ceiling' on the amount of cortisol a laboratory stressor can produce may explain why participants in the sleep deprivation condition demonstrated blunted cortisol responses.

1. Introduction

While individual sleep need varies widely from person to person, most sleep experts recommend 7 to 9 h of sleep per night (Hirshkowitz et al., 2015). Yet, nearly 30% of adults sleep 6 or fewer hours per night (Krueger and Friedman, 2009). These rates are concerning as sleep deprivation is linked to a number of negative health outcomes, including psychiatric (Breslau et al., 1996), metabolic (Knutson et al., 2007), and cardiovascular problems (Grandner et al., 2013). However, the actual mechanisms by which sleep deprivation impacts health are relatively unknown. Growing research points to variability in neuroendocrine functioning, in particular the hypothalamic-pituitary-adrenal (HPA) axis, as a potential mechanism by which sleep deprivation leads to poor health (Balbo et al., 2010; Meerlo et al., 2008). Yet, experimental studies on the association between sleep deprivation and HPA-axis functioning, in particular cortisol stress reactivity, are limited (Minkel et al., 2014). Accordingly, the current study explored the link between acute sleep deprivation and HPA-axis stress reactivity under controlled conditions.

The HPA axis' primary function is to regulate physiological responses to stress (de Kloet, 1991; Johnson et al., 1992). HPA-axis stress reactivity is, however, also modulated by several individual (e.g., age, gender; Kudielka et al., 2004a) and contextual factors (e.g. time of day; Kudielka et al., 2004b). Among these factors, sleep may play a critical role in modulating HPA-axis stress reactivity (Sgoifo et al., 2006). Several studies suggest that poor sleep is associated with atypical cortisol reactivity to psychosocial stress among both children (Hatzinger et al., 2008; Räikkönen et al., 2010) and adults (Wright et al., 2007). Specifically, poor self-reported sleep quality has been linked to elevated cortisol responses to a laboratory stress task (Goodin et al., 2012). Similarly, among children and adoles-

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http://dx.doi.org/10.1016/j.psyneuen.2017.01.030
0306-4530/

cents, lower objective (e.g., lower sleep efficiency, more time spent in 'light' stages of sleep) and subjective sleep quality predicted greater overall cortisol production in response to stress (Hatzinger et al., 2008; Mrug et al., 2016; Räikkönen et al., 2010). A more recent study among a small sample of healthy adults used an experimental paradigm to demonstrate a link between acute (i.e., total) sleep deprivation and elevated cortisol responses to a laboratory stressor (Minkel et al., 2014). Poor or insufficient sleep may increase adrenal sensitivity, and thus exacerbate cortisol production during acute stress. For example, following a 48 h sleep deprivation protocol, sleep deprived rodents showed blunted adrenocorticotropic hormone (ACTH) compared to controls, whereas glucocorticoid (i.e., cortisol) production was not significantly different between the two groups (Sgoifo et al., 2006). Accordingly, under sleep-deprived conditions, less ACTH may be needed to signal the appropriate release of glucocorticoids in response to stress.

Alternatively, other studies have demonstrated a link between poor sleep and a blunted cortisol response to acute stress (Capaldi et al., 2005; Wright et al., 2007). These inconsistencies further highlight the need to identify the specific mechanisms by which poor sleep is responsible for atypical HPA-axis functioning. For example, poor sleep may be due to elevated physical or mental health symptoms that may be differentially related to high and low stress reactivity. However, to date, only one study has examined the impact of experimental sleep deprivation among humans (Minkel et al., 2014), and therefore, it is relatively unknown whether sleep deprivation actually leads to differences in HPA-axis stress reactivity. Addressing this question is important because it is possible that sleep deprivation and HPA-axis functioning are not directly related and are instead due to a third variable, such as high levels of stress (Sadeh and Gruber, 2002; Sadeh et al., 2004) or the presence of comorbid psychiatric symptoms (Ivanenko et al., 2006). However, experimentally controlled sleep deprivation has been consistently linked to elevated *circadian* cortisol (i.e., greater nocturnal cortisol during sleep deprivation and higher post-deprivation evening cortisol; Leproult et al., 1997; Treuer et al., 2007), and thus it is possible that sleep deprivation directly impacts other indices of HPA-axis functioning (e.g., stress reactivity) as well.

Therefore, the current study investigated the relationship between total sleep deprivation and HPA-axis stress reactivity under experimental conditions. We hypothesized that sleep deprivation would be associated with greater cortisol in response to stress, given the demonstrated links between poor sleep and increased HPA-axis stress reactivity (Goodin et al., 2012; Hatzinger et al., 2008; Räikkönen et al., 2010). Specifically, we aimed to extend Minkel et al.'s (2014) findings and provide further support for the link between acute sleep deprivation and HPA-axis sensitivity to stress, which may have treatment implications for a variety of conditions linked to an elevated cortisol stress response (e.g., depression; Burke et al., 2005).

2. Methods

2.1. Participants

Participants included 45 young adults (22 females; M_{age} = 22.6, SD_{age} = 3.1) recruited from the local community of a mid-size city in the United States. Participants were recruited through online and printed advertisements placed in local businesses and community centers seeking "healthy" young adults for a sleep study. Participants were ineligible for participation if they were (1) pregnant, (2) taking any medication that impacts endocrine functioning, (3) previously diagnosed with a chronic medical condition (e.g., sleep apnea, cancer, lupus, diabetes), endocrine disorder (e.g., Cushing's syndrome, Addison's disease), or a psychiatric disorder (including insomnia), or (4) unable to maintain a regular sleep cycle during the week prior to the overnight visits (e.g., shift worker). All participants were able to maintain a regular sleep cycle, and therefore, no participants were excluded for this reason. Five participants (2 females; M_{age} = 21.8, SD_{age} = 3.4) dropped out before completing all the parts of the study, and were therefore excluded from the current analyses. The final sample included 40 participants (20 females; M_{age} = 22.7, SD_{age} = 3.1). There were no significant differences between the five participants who did not complete the study and the remaining sample on age ($F = 0.34$, $p > 0.20$), depressive symptomatology ($F = 1.15$, $p > 0.20$), perceived stress ($F = 0.59$, $p > 0.20$), life events ($F = 1.78$, $p = 0.19$), insomnia symptoms ($F = 0.12$, $p > 0.20$), daytime sleepiness ($F = 0.04$, $p > 0.20$), self-reported habitual sleep quality ($F = 0.05$, $p > 0.20$), or chronobiological preference ($F = 1.29$, $p > 0.20$). The majority of participants in the final sample identified as Caucasian (57.5%). The remaining sample was composed of 20.0% African American, 12.5% Asian American, and 2.5 Biracial. 12.5% of the sample identified as Hispanic. 75% of the sample included full-time college students (undergraduate or graduate students). The Institutional Review Board of a large American research university approved the study, and participants signed a written informed consent.

2.2. Procedures

2.2.1. Baseline laboratory visit

During the baseline visit, each participant completed a series of questionnaires about their sleep habits. Specifically, these questionnaires assessed general sleep patterns (Pittsburgh Sleep Quality Index; Buysse et al., 1989), daytime sleepiness (Epworth Sleepiness Scale; Johns, 1991), chronobiological preference (Morningness-Eveningness Questionnaire; Horne and Ostberg, 1976), and insomnia symptoms (Insomnia Severity Index; Morin, 1993). Participants also completed a general demographic questionnaire that included other sleep-related information (e.g., habitual caffeine use). Following the baseline visit, participants wore an actigraphy device (Actiwatch 2, Philips – Respironics) on their non-dominant wrist for approximately seven days (range = 2–11 days). The actigraph is a widely used method for objectively assessing daily sleep/wake patterns (Sadeh et al., 1994). In addition, on each day actigraphy data was collected, participants were asked to complete a brief online sleep diary (modified Consensus Sleep Diary; Carney et al., 2012). Participants were instructed to maintain a regular sleep/wake schedule (i.e., 7–8 h of sleep per night; morning waking time between 06:00-09:00) and abstain from napping during the subsequent week. Actigraphy and sleep diary data were used to estimate each participant's habitual (i.e., average) sleep patterns during the week prior to the overnight laboratory visit. While not all participants were able to provide a week's worth of actigraphy and diary data due to scheduling limitations, there were no significant difference in the number of days collected between conditions, $F = 0.003$, $p > 0.20$; sleep deprivation, M_{days} = 7.32, sleep controls, M_{days} = 7.35. The adaptation night was not included in these estimates since they were given a predetermined bed and rise time. Sleep efficiency, total sleep time, and other sleep continuity variables (e.g., wake after sleep onset, nocturnal awakenings) are sensitive to first night effects (Agnew et al., 1966), and therefore, not representative of habitual sleep patterns. Notably, there were no significant group differences on any of the actigraphy-measured sleep variables during the adaptation night. The following sleep parameters were used as covariates for the current analyses: total sleep time (TST), sleep efficiency (SE), sleep onset latency (SL; how long it took them to initiate sleep, in minutes), wake after sleep onset (WASO; sum of their nocturnal awakenings, in minutes), and nocturnal awakenings (NWAK; number of awakenings).