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Sex differences in perceptions of sleep inertia following nighttime awakenings

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Abstract

Study Objectives: The influence of biological sex on sleep inertia symptoms is currently unknown. We investigated the role of sex differences in the subjective experience and objective cognitive manifestation of sleep inertia following nighttime awakenings.

Methods: Thirty-two healthy adults (16 female, 25.91 ± 5.63 years) completed a 1-week at-home study with one experimental night during which sleep was measured by polysomnography and participants were awakened during their habitual sleep time. Participants completed a psychomotor vigilance task, Karolinska Sleepiness Scale (KSS), visual analog mood scales, and a descending subtraction task (DST) prior to sleep (baseline) and at 2, 12, 22, and 32 min after awakening. A series of mixed-effects models with Bonferroni-corrected post hoc tests were used to examine the main effects of test bout and sex, and their interaction, with a random effect of participant, and order of wake-up and sleep history as covariates.

Results: All outcomes except for percent correct on the DST showed a significant main effect of test bout, with worse performance after waking compared to baseline (all *p*s < .003). Significant effects of sex ($p = .002$) and sex × test bout ($p = .01$; $R^2_M = 0.49$, $R^2_C = 0.69$) were observed for KSS, with females reporting a greater increase in sleepiness from baseline to after waking compared to males.

Conclusions: These results suggest that while females reported feeling sleepier than males following nighttime awakenings, their cognitive performance was comparable. Future research is needed to determine whether perceptions of sleepiness influence decision-making during the transition from sleep to wakefulness.

Key words: alertness; sleepiness; on-call; vigilant attention; working memory

Statement of Significance

Our findings are the first to describe a sex difference in the perception of sleepiness after waking from nighttime sleep. Under conditions simulating an on-call awakening at night, females rated their sleepiness as greater than males. Cognitive performance, however, as assessed by a vigilant attention and working memory task, did not differ between females and males. Our research elucidates novel individual differences in sleep inertia that could be important for tailoring fatigue management guidance for on-call workers required to perform safety-critical tasks soon after waking. Future research is required to explore the physiological—or psychological—mechanisms underlying the observed sex profiles of the neurobehavioral experience of sleep inertia.

Introduction

Sleep inertia refers to the brief impairment of alertness, mood, and cognitive performance experienced during the transition from sleep to wakefulness [1]. Although several state factors such as time of day [2], prior sleep-wake history [3], and sleep stage at waking [4] can influence the severity of sleep inertia, individual trait variation may also contribute to this experience [5].

A recent study found that the magnitude of self-reported sleepiness after waking varies by individual as a trait, even following different sleep-wake histories [5]. Furthermore, this variation in

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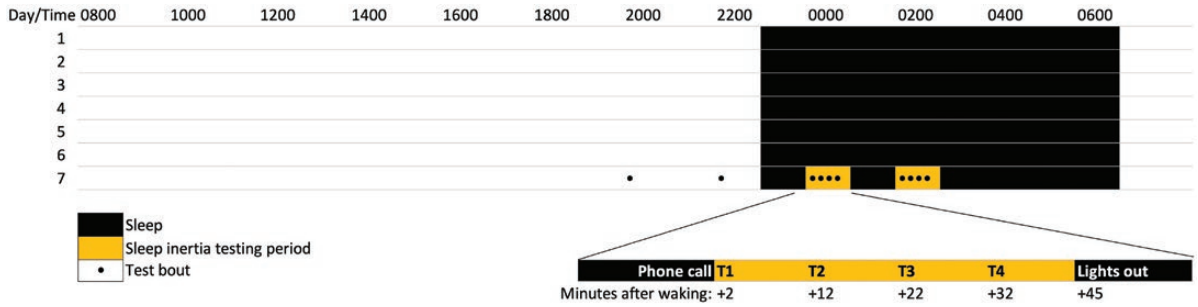

Figure 1. Protocol schematic. Times shown are approximate as participants followed habitual sleep times. Night 6 was the adaptation night in which participants wore the polysomnography equipment and kept the same sleep-wake schedule as night 7. Night 7 was the experimental night during which baseline tests were performed prior to sleep and participants were awoken with a phone call to begin sleep inertia testing. The order of the control wake-up session (first or second wake-up) was randomized by sex. Data from the intervention wake-up session are not presented here.

sleep inertia magnitude was not associated with individual differences in vulnerability to sleep loss. While this study provides unique insight into the trait-like nature of sleep inertia, questions remain regarding the impact of individual traits on objective outcomes of sleep inertia and the role of biological sex as a trait factor.

Exploring potential sex differences in established physiological and psychological responses is critical to informing guidance for females following decades of male participant-dominated research [6]. In the sleep and circadian literature, sex differences have been found related to sleep duration, timing, and architecture [7–9], circadian timing and amplitude [8, 10], and chronotype [11]. To the best of our knowledge, however, the role of sex in sleep inertia has yet to be investigated.

Identifying individuals at greater risk of sleep inertia is important in on-call and sustained operations schedules in which workers may be required to perform a safety-critical task soon after waking. Recognizing individual differences in the response to abrupt awakening in real-world scenarios can help tailor guidance in the workplace. Therefore, we aimed to assess the influence of sex differences on subjective alertness and mood, and objective cognitive performance immediately after waking from nighttime sleep in an at-home setting.

Methods

Participants

Healthy adults were recruited for the study based on self-reported health and sleep habits including absence of known medical or psychiatric conditions (Body Mass Index 18–30, General Health Screening Questionnaire, Beck Depression Inventory, State-Trait Anxiety Inventory, Symptoms Checklist 90R), habitual sleep of 6–9 h, bedtime between 21:00 and 03:00, and waketime between 06:00 and 12:00. Participants were asked to abstain from illicit substances, nicotine, and alcohol for the duration of the study. Naps were not allowed on the day of the experimental night. Caffeine was allowed up until two hours after waking on the morning of the experimental night (i.e., all tests were performed at least 11 h after the last caffeine opportunity). Participants completed a series of non-exclusionary demographic questionnaires including the Pittsburgh Sleep Quality Index, Epworth Sleepiness Scale, Morningness-Eveningness Questionnaire, and Fatigue Severity Scale. Informed consent was obtained via video conferencing and electronic signature prior to participation in the study. The study protocol was approved by the NASA Institutional Review Board (STUDY00000335).

Protocol

The study was performed at each participant's home with no laboratory visits. All equipment was dropped off and picked up following COVID-19 distancing and sanitation guidelines. See Figure 1 for an overview of the protocol.

Participants wore an activity monitor (Actiwatch Spectrum PRO, Philips Respironics, Murrysville, PA, USA) during their normal sleep-wake schedule for six nights ahead of the experimental night. Participants worked with the recruiter to pre-select bed and wake times for the habituation and experimental night (nights 6 and 7) that met our criteria (between 9 pm and 3 am bedtime, at least 6 h of time-in-bed) and were based on their habitual bedtimes. On night 6, researchers worked remotely with participants via a swivel-mounted, one-way, infrared camera to set up and test experimental equipment, familiarize participants with experimental procedures, practice cognitive tasks, and adapt to sleeping with the polysomnography equipment. At the participant's habitual bedtime on nights 6 and 7, lights were turned off and the participant was instructed to try to sleep until a researcher called them on the provided study phone. The ringtone, volume, and screen brightness were preset according to experimental criteria and confirmed on each study night. On night 6, participants had an uninterrupted sleep period and were not called until their habitual waketime the next morning.

On the experimental night (night 7), participants performed baseline testing sessions at two hours and one hour before bedtime under remote observation. Following baseline testing, polysomnography equipment was applied and tested. Participants were informed that they would receive at least one wake-up call during the night and to follow the researcher's instructions when they received a call. The camera was turned away from participants during sleep opportunities.

At 45 min and 135 min after bedtime, participants received a phone call and were instructed to sit up on the side of their bed and turn on the dim, red light provided. The camera was rotated to view the participant during the awakening and the testing session which included a test bout performed at 2 (T1), 12 (T2), 22 (T3), and 32 (T4) min after the phone call. Participants were then instructed to go back to sleep. The results presented here are the control arm (i.e., unmitigated sleep inertia) of an intervention study with condition order randomized by sex.

Test battery

Vigilant attention was measured using a 5-minute psychomotor vigilance task (PVT) performed on the NASA PVT + application (iPod 6th generation; iOS v.12.5.3; NASA PVT + v.1.4.1 B.1999).

Table 1. Participant demographics

	All	Female	Male	*p*	*d*
Mean (SD)					
Age (years)	25.91 (5.63)	25.44 (5.49)	26.38 (5.91)	.65	−0.16
PSQI	3.41 (1.19)	3.06 (1.18)	3.75 (1.13)	.10	−0.60
MEQ	51.84 (7.84)	53.07 (8.25)	50.69 (7.52)	.41	0.30
ESS	5.13 (2.43)	5.20 (2.54)	5.06 (2.41)	.88	0.06
n					
Total *N*	32	16	16	—	—
White	17	8	9	—	—
Asian	17	8	9	—	—
Native Hawaiian/Pacific Islander	2	1	1	—	—

Participants could choose more than one race/ethnicity, therefore, totals may exceed the total sample size.
PSQI, Pittsburgh Sleep Quality Index; MEQ, Morningness-Eveningness Questionnaire; ESS, Epworth Sleepiness Scale.

Outcomes of interest included response speed (1/reaction time [RT]) and number of lapses (RT > 500 ms) [12, 13]. Following the PVT, subjective alertness and mood were assessed using the Karolinska Sleepiness Scale (KSS) and nine visual analogue scales (VAS) of mood (alert–sleepy, cheerful–miserable, calm–tense, depressed–elated, stressed–relaxed, peaceful–hostile, greedy–generous, aggressive–easygoing, lethargic–energetic). Working memory was measured using a 3-minute descending subtraction task (DST) described elsewhere [4]. Outcome measures of interest included total number of responses (total responses), total number of correct responses (total correct), and percentage of correct responses (percent correct).

Sleep

Sleep was monitored using the Prodigy head mount unit (Cerebra Health Inc, Winnipeg, Canada) [14] which included eight electrodes: two prefrontal electrodes (positioned at approximately Fp1, Fp2), two eye electrodes (positioned 1 cm outside and below the right canthus and above the left canthus), one chin electrode (electromyogram), two ground/bias (positioned at approximately Fp_z), and one reference (left mastoid). Sleep was preprocessed using Prodigy default filters [15] and scored by a single-blinded Registered Polysomnographic Technologist using American Academy of Sleep Medicine rules [16].

Analysis

Welch-corrected *t*-tests and Mann–Whitney *U*-tests were used to assess demographic and sleep metrics between sexes. A chi-square test of independence was used to evaluate differences in sleep stage at awakening. A series of linear mixed-effects models with Bonferroni-corrected post hoc tests were performed with fixed effects of test bout (baseline, T1–T4), sex (female, male), test bout × sex, and a random effect of participant. Randomization order and actigraphically estimated sleep history across the prior six nights were included as covariates. One participant's sleep history was estimated based on sleep diaries due to an actiwatch failure. Linear models were implemented in the analyses of KSS, mood, and PVT response speed. A negative binomial model was specified for the analysis of number of PVT lapses. A Poisson model was used for total responses and total correct on the DST, while percent correct was arcsine-transformed and analyzed using a linear model. For all models, we computed marginal and conditional values for R^2 to reflect the variance explained by the fixed effects alone, as well as the combined impact of the fixed and random effects, respectively [17].

Results

Thirty-six participants (18 female) completed the study. Data from two female participants were excluded because they were already awake at the time of the wake-up call; one male participant's data were excluded due to noncompliance; and one participant's data were excluded due to identifying as nonbinary. A final sample of $N = 32$ (16 female) was included in the analysis. Table 1 displays the participant demographics. There were no significant sex differences for any of the collected demographic variables (all *p*s > .05).

Of the female participants, $n = 4$ (25%) were currently using birth control and $n = 13$ (81%) reported having regular menstrual cycles. Menstrual phase was estimated from the self-reported date of menses onset and average length of cycle (29.2 ± 2.4 days), with $n = 6$ (38%) in the follicular phase (defined as the first half of average cycle length) and $n = 7$ (44%) in the luteal phase (defined as the second half). We were unable to estimate phase for $n = 3$ (19%) due to irregular cycles. For example, if the participant reported an average cycle length of 30 days, days 1–15 would be considered follicular phase, and days 16–30 would be considered luteal (with day 1 the reported date of menses onset). These menstrual phase estimates are reported as an approximate guide but were not accurate enough to warrant inclusion in the models.

Sleep

There were no significant differences between sexes for the average total sleep time across the six nights preceding the experimental night ($p = .39$) as measured by actigraphy. Sleep timing varied *between* participants but was relatively consistent *within* participants across the week. For example, the standard deviation of bedtimes within participants across the study week was 33.2 min, whereas the standard deviation of average bedtimes between participants was 56.1 min. Nine participants napped during the prior week ($n = 5$ female) with an average ~2 naps each. Visualizing the sleepiness data for these individuals relative to the whole sample, there were no obvious trends differentiating them from the larger group.

There were no significant differences in polysomnographically recorded sleep architecture in the 45-minute sleep opportunity

Table 2. Sleep history (nights 1–6) and sleep architecture of the 45-minute sleep opportunity preceding sleep inertia testing (night 7)

		All	Female	Male	*p*	ES
Nights 1–6	TST*	462.35 (33.35)	467.49 (33.00)	457.22 (33.96)	.39	0.31
Night 7	W	13.00 (11.38)	15.25 (10.63)	11.50 (15.50)	.75	0.07
	N1	5.50 (4.25)	5.75 (4.00)	5.50 (5.13)	.84	0.05
	N2	8.25 (4.50)	9.25 (3.63)	7.50 (7.75)	.17	0.29
	N3	12.25 (18.13)	14.00 (12.38)	7.50 (21.13)	.33	0.21
	REM	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	—	—
	TST	31.25 (12.25)	29.50 (10.88)	33.25 (16.00)	.69	0.09
	SOL	10.75 (11.13)	15.25 (9.88)	8.25 (13.63)	.52	0.14
	WASO	0.50 (1.88)	0.00 (0.63)	1.00 (3.00)	.09	0.34
Sleep stage at awakening (*n*)	N1	4	2	2	.72	—
	N2	9	4	5		—
	N3	18	10	8		—
	REM	1	0	1		—

ES, effect size; W, wake; N1, N2, N3, stage non-REM 1, 2, 3; REM, rapid eye movement; TST, total sleep time; SOL, sleep onset latency; WASO, wake after sleep onset. *Denotes average of actigraphic sleep estimate with Welch's *t*-test conducted for the comparison between sex; mean (standard deviation) and Cohen's *d* reported. For all metrics excluding total sleep time for Nights 1–6, median minutes (interquartile range) and the rank biserial correlation for the comparison between sex are reported.

prior to awakening (all *p*s > .05), nor the sleep stage that participants were awakened from, $\chi^2(3, n = 32) = 1.33$, $p = .72$ (see Table 2). Participants slept for 31.25 ± 12.25 min (median minutes ± interquartile range) in the 45-minute sleep opportunity and the majority were awakened from N3 ($n = 18$, 56%).

Sleepiness, mood, and cognitive performance

All subjective and objective outcome metrics, except for percent correct on the DST ($p = .39$; $R^2_M = .03$, $R^2_C = .79$), showed a significant main effect of test bout, with worse performance after waking compared to pre-sleep baseline (all *p*s < .006; all $R^2_M > .08$, all $R^2_C > .53$). A significant effect of sex was observed for KSS ($p = .002$; $R^2_M = .49$, $R^2_C = .69$) and VAS_{alert} ($p = .02$; $R^2_M = .35$, $R^2_C = .55$), and a significant interaction effect for KSS ($p = .01$), with females reporting a greater increase in sleepiness from presleep to after waking compared to males (Figure 2A). There were no sex nor test bout × sex effects for any other subjective mood or objective performance outcome metrics (all *p*s > .05; see Figure 2B–D).

Discussion

Our study is the first to explore sex differences in the subjective experience and cognitive performance impacts of sleep inertia. Our results suggest that while females report feeling sleepier following awakening at night, their cognitive performance is similar to males. Further research is needed to determine the influence of self-assessed sleepiness on decision-making behavior during this potentially critical post-awakening period.

Specifically, we observed that after being abruptly awakened from a habitual sleep period, females rated themselves as sleepier, but did not differ on tasks of vigilant attention and working memory, relative to males. In a previous study of self-rated performance during the sleep inertia period, participants were found to over-estimate their cognitive performance with self-ratings of improved performance after a short nighttime nap despite significant performance impairments due to sleep inertia [13]. Interestingly though, participants in that study reported no change in subjective sleepiness on the KSS after waking, suggesting that self-rated sleepiness and self-rated performance are not necessarily associated during the sleep inertia period. The previous study [13] employed a mixed cohort, but sex differences were not reported due to a small sample size. It may be tempting to conclude that females are more accurate in estimating their sleepiness during the sleep inertia period relative to males. However, there was also an increase in sleepiness ratings following awakening for males, albeit to a lesser magnitude than females. It is unclear from our data which sleepiness estimate is more "accurate" relative to objective sleepiness and cognitive performance impairment. Further research is needed to determine whether perceptions of sleepiness influence perceived ability and subsequent decision-making during the transition period from sleep to wake and the potential influence of sex differences on these behaviors.

Lundholm *et al.* [5] recently described a trait-like factor in the subjective experience of sleep inertia. Our results suggest that sex may be a contributory factor to this trait experience. Given the incongruency between subjective and objective outcomes by sex in our study, it remains to be seen whether the trait-like subjective experience reported by Lundholm *et al.* extends to objective cognitive performance. Another study that reported only subjective sleep inertia experiences via the Sleep Inertia Questionnaire [18] found no differences between males and females when comparing several network properties of the questionnaire. This finding suggests that, contrary to our findings, the overall subjective experience of sleep inertia between males and females is similar. However, on the single item that best matches the KSS (i.e. "Notice that you feel sleepy?"), females self-reported significantly higher values than males, albeit the effect size was small.

Chronotype is a known contributing factor to sleep inertia severity [19], and females in the age range of our cohort are typically more morning type than males [11]. Our results, however, are unlikely to be influenced by chronotype as there were no significant differences in chronotype between our male and female participants. Our experimental design also accounted for any

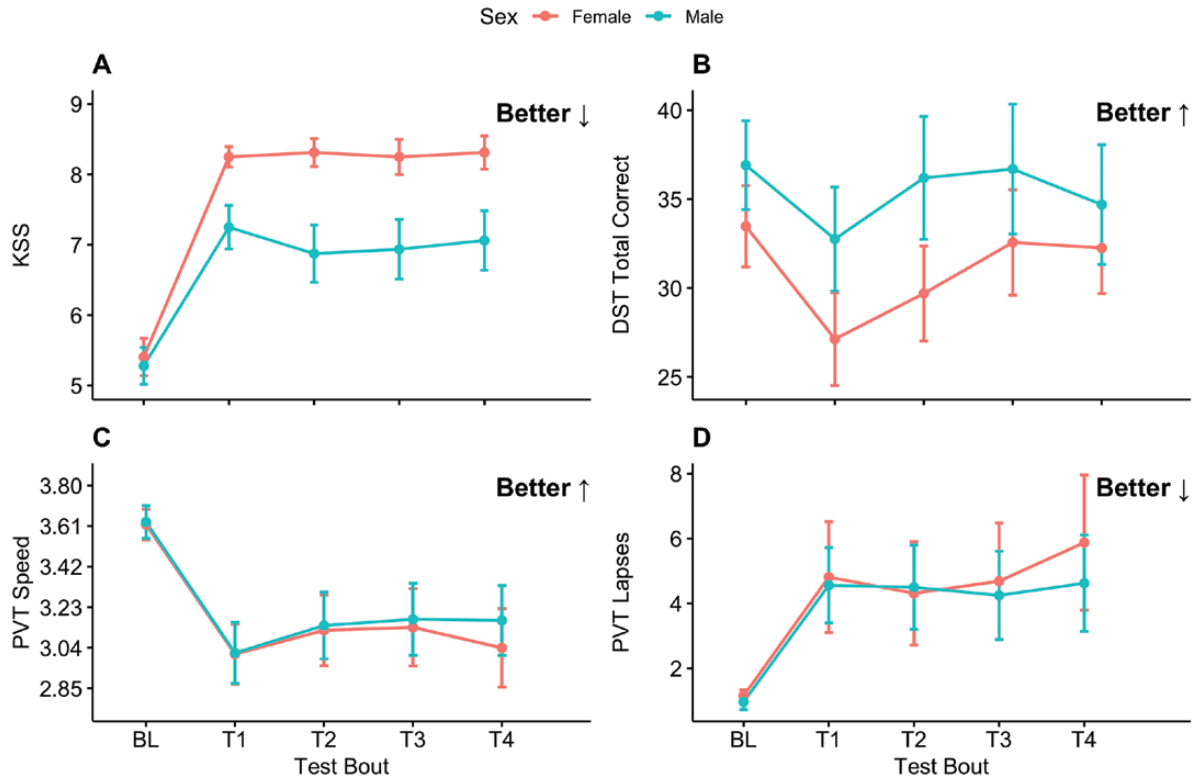

Figure 2. Neurobehavioral outcomes across test bouts by sex (F = female [salmon], M = male [teal]). (A) Karolinska Sleepiness Scale (KSS); (B) Descending subtraction task (DST) total number of correct responses; (C) Psychomotor Vigilance Task (PVT) response speed; and (D) PVT lapses. BL = pre-sleep baseline.

subtle differences in chronotype by aligning sleep time to each participant's self-selected habitual bedtime. The influence of chronotype may, however, be more apparent during other waking scenarios such as forced early morning awakenings. Despite these controls, it is possible that tests were performed at a later circadian phase in females as they typically have a longer phase angle than males [10]. Additional research is necessary to determine circadian phase during testing and whether our results extend to other scenarios such as waking at different times of day.

Our randomized crossover study of sex differences in subjective and objective sleep inertia outcomes following polysomnographically recorded sleep is not without limitation. First, given the real-world setting of the study, we were unable to control the sleep stage from which participants were awakened. There were, however, no significant sex differences for sleep architecture, sleep stage prior to awakening, or total sleep time in the prior six nights, which suggests that our results are not due to an imbalance in sleep history between the two groups. Second, we only have a crude estimate of menstrual phase for our female participants. These estimates suggest that female participants were relatively evenly distributed across menstrual phases known to influence nighttime neurobehavioral performance [20, 21]. Although menstrual phases have been shown to influence sleep [22], we did not see a difference in sleep between sexes, suggesting that our results are unlikely to be due to secondary impacts of menstrual phase on sleep itself. Further research is needed to investigate the potential influence of menstrual phase on sleep inertia symptoms and ratings of sleepiness in women. Finally, although we were able to detect differences in sleepiness between sexes, we may have been underpowered to detect a difference in working memory (as assessed by DST). Visual inspection of the plots reveals a potential sex difference on DST outcomes but not PVT outcomes. Importantly, the working memory data do not suggest an interaction effect of sex × test bout (which might indicate a sleep inertia-specific sex difference), but rather show a consistent sex difference across test bouts including the pre-sleep baseline, which was not the focus of our study.

Conclusion

Investigating individual differences in neurobehavioral responses to sleep inertia advances our understanding of the sleep-wake transition and allows for evidence-based tailoring of fatigue management programs. Our results provide new evidence in this area and suggest that sex differences may play a role in the subjective experience of sleep inertia, but do not appear to drive differences in vigilant attention or working memory post-awakening.

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Disclosure statement

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Data Availability Statement

Data are accessible upon reasonable request as far as allowed by the data sharing policy and guidelines established by NASA Ames Research Center.

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