A Micro-Longitudinal Study of Naps, Sleep Disturbance, and Headache Severity in Women with Chronic Migraine

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ABSTRACT

Objective: To examine the relationship between headaches, naps, and nocturnal sleep in women with chronic migraine (CM) using micro-longitudinal data from diaries and actigraphy.

Methods: 20 women with CM and 20 age and sex-matched healthy controls (HC) completed self-report questionnaires, electronic diaries, and wrist actigraphy over a 4-week period. Between-group comparisons were conducted with naps (frequency and duration) as the primary variable of interest. Within-group analyses were conducted on the CM group using hierarchical linear mixed models to examine the temporal relationships between headache severity, sleep behaviors, and sleep parameters. The primary variables of interest were naps (number and duration) and nocturnal sleep efficiency (diary and actigraphy).

Results: The CM group reported significantly more days with naps (25.85%) compared to the HC group (9.03%) during the study period (p=.0025). Within-group analyses in CM revealed that greater headache severity was associated with longer nap duration (p=.0037) and longer nap duration was associated with lower sleep efficiency measured using diaries (p=.0014) and actigraphy (p<.0001).

Conclusions: Napping is more frequent in CM than HC and nap duration in CM is associated with headache severity and nocturnal sleep disturbance. These findings provide initial support for the hypothesis that daytime napping is a behavioral coping strategy used in CM that could contribute to insomnia.

Key Words: migraine, sleep, insomnia, naps, actigraphy, women

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INTRODUCTION

Sleep disturbance is prominent in chronic migraine (CM) and is implicated as a risk factor in headache exacerbation. Poor sleep has been found to precede migraine headaches (Andress-Rothrock, King, & Rothrock, 2010; Boardman, Thomas, Millson, & Croft, 2006; Kelman & Rains, 2005; Odegard et al., 2011; Pellegrino, Davis-Martin, Houle, Turner, & Smitherman, 2018) but other studies have found inconsistent or contrary results (Bertisch et al., 2020; Blau, 1982; Kikuchi, Yoshiuchi, Yamamoto, Komaki, & Akabayashi, 2011). Findings are further limited by methodological issues including reliance on self-report measures and inconsistencies in characterizing the type of sleep disturbance (for a critical review see (Ong & Park, 2012). As a result, the relationship between sleep and migraine remains unclear and new approaches are needed.

Compared to nocturnal sleep, daytime naps have been understudied in migraine. Naps are often used as a behavioral coping strategy for headaches (Haque et al., 2012; Ong, Stepanski, & Gramling, 2009), but models of insomnia have demonstrated that daytime naps can contribute to the development and maintenance of insomnia (Spielman, Caruso, & Glovinsky, 1987). It has been posited that people with CM who frequently take naps as a headache-coping strategy could be at risk for developing a comorbid insomnia disorder (Ong & Park, 2012). To our knowledge, the impact of daytime naps on nighttime sleep and next-day headaches has not been specifically examined in CM.

The purpose of this study was to examine the relationship between headaches, sleep behaviors, and sleep parameters in women with CM using micro-longitudinal data from diaries and wrist actigraphy. This study focused on women because the rate of migraine is three to four times higher compared to men (Al-Hassany et al., 2020) and women are at higher risk for

insomnia than men (Ohayon, 2002). The goal was to explore the hypothesis that napping is a

common behavior in CM and could play an important role in the link between headaches and

insomnia. Specifically, we hypothesized that: 1) women with CM take more frequent naps than

matched healthy controls, 2) napping in CM is temporally associated with more sleep

disturbance at night as indicated by lower sleep efficiency, and 3) lower sleep efficiency in CM

is temporally associated with next-day headache severity. In addition to these main hypotheses,

we explored the relationship among headache severity, sleep, and other sleep behaviors relevant

to insomnia.

METHODS

Participants

Participants were 40 females between the ages of 18 and 40 without signs of perimenopause.

Participants were primarily recruited from the community through posted advertisements, flyers,

and emails sent to a women's health registry list. Eligibility screening consisted of a telephone

interview followed by an in-person interview that included a review of medical history,

structured diagnostic interviews for headache (Andrew, Penzien, Rains, Knowlton, & McAnulty,

1992), sleep disorders (Edinger et al., 2011), and psychiatric conditions (First, 1995). Diagnosis

of migraine was confirmed by review of symptoms and a medical exam with the study

neurologist.

Women in the CM group met the International Classification of Headache (3rd edition)

for CM (2018). Participants with CM were age-matched (+/- 3 years) to a participant in the

healthy control (HC) group who had no history of headache disorder and ≤ 1 headache day per

month in the past 12 months. Exclusion criteria for both groups included unstable medical or

psychiatric conditions that would interfere with the study protocol or require immediate

treatment, regular use of illegal substances or medications known to affect sleep or melatonin,

pregnancy or nursing, engagement in night shift work, and travel across more than three time

zones in the month prior to enrollment (see supplement 1 for details). The study was approved by

the Institutional Review Board at Rush University Medical Center and all participants provided

written informed consent prior to participation.

Measures

Self-Report Questionnaires

        Several self-reported measures commonly used in the clinical assessment of migraine or

sleep disorders were collected to evaluate the clinical profile of the sample. The Pittsburgh Sleep

Quality Index (PSQI) (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) and Insomnia

Severity Index (ISI) (Bastien, Vallieres, & Morin, 2001) are standard measures that assess global

symptoms of sleep disturbances and daytime dysfunction related to sleep and include validated

cut-offs for clinically significant symptoms of insomnia. The Pre-Sleep Arousal Scale (PSAS)

(Nicassio, Mendlowitz, Fussell, & Petras, 1985), Hyperarousal Scale (Pavlova et al., 2001),

Dysfunctional Beliefs and Attitudes about Sleep (DBAS) (Morin, Stone, Trinkle, Mercer, &

Remsberg, 1993), and Ford Insomnia Response to Stress Test (FIRST) (Drake, Richardson,

Roehrs, Scofield, & Roth, 2004) were used to assess cognitive and emotional factors related to

insomnia. The Fatigue Severity Scale (FSS) (Krupp, LaRocca, Muir-Nash, & Steinberg, 1989)

and Epworth Sleepiness Scale (ESS) (Johns, 1991) were used to assess the associated daytime

impairment related to sleep disturbances. In addition to these measures, demographic data and

the number of migraine days per month (30 days) were collected during the screening visit.

Sleep and Headache Diaries

Prospective daily diaries were used to measure self-reported sleep and headache activity

throughout the study duration via a secure website designed for this study. For sleep behaviors,

participants were asked about the following items: the time of getting into bed at night, bed time

(time intending to go to sleep), rise time (time getting out of bed in the morning), and the number

and duration of naps during the day. For sleep parameters, participants were asked to report sleep

onset latency (SOL), wake after sleep onset (WASO), and total sleep time (TST). Time in bed

(TIB; calculated as the duration from bed time to rise time), total wake time (TWT; calculated as

SOL + WASO), total sleep time (TST; calculated as TIB minus TWT), and sleep efficiency (SE

= TST/TIB x 100) were derived from these sleep parameters. The sleep items follow the

recommendations for a standardized sleep diary (Carney et al., 2012) and are considered to be

the standard of practice for self-reported measurement of sleep/wake patterns (Buysse, Ancoli-

Israel, Edinger, Lichstein, & Morin, 2006). Maximum headache severity was assessed each day

on a 0-10 scale (0=no headache, 10=most severe headache). Participants were asked to complete

each diary entry within one hour of their rise time based on the activities of the previous

day. Each entry was time-stamped and reviewed by the research team to minimize recall bias. To

minimize missing data, participant compensation was reduced if they missed more than two days

of diary entries.

Actigraphy

Wrist actigraphy (Actiwatch Spectrum, Phillips Respironics, Bend, OR) was used to measure

objective sleep/wake patterns concurrent with the sleep diaries throughout the study period.

Actigraphy is commonly used to assess longitudinal sleep/wake patterns and has been well-

validated as an objective measure of sleep (Buysse et al., 2006). Participants were instructed to

wear the actigraph on the non-dominant hand during the day and night, using the event marker

on the device to indicate bed time and rise time. Rest intervals were manually set according to a

pre-established protocol used in previous studies (see supplement 2 for details) (Ong et al., 2014;

Ong, Taylor, et al., 2018). Data were analyzed in 60 second epochs using medium sensitivity for

determining wakefulness with Respironics Actiware version 6.0.

Procedure

The present study is an observational, micro-longitudinal study examining the self-reported

diaries and actigraphy data collected as part of a previously published study (Ong, Taylor, et al.,

2018). A total of 65 potential participants were screened for eligibility with 24 CM and 20 HC

qualifying the study. Two CM participants did not complete the assessment protocol and two

other CM participants were unmatched, resulting in the final sample size of 20 CM and 20 HC.

The study duration (mean = 28.20 days, SD = 3.16 days, range = 21-36 days) was

selected to include one complete menstrual cycle or 28 days for women who did not have a

regular menstrual cycle (i.e., due to IUD, continuous hormonal birth control, or hysterectomy).

The number of days observed was not significantly different between the CM (M=28.20,

SD=3.44) and HC (M=27.55, SD=2.80) groups. Following a brief orientation upon determining

eligibility, participants were provided with instructions for the at-home monitoring protocol,

which included how to use the actigraph and the online sleep/headache diary, beginning on day 1

of their menstrual cycle and continuing until the start of the next menstrual cycle. Participants

completed an in-lab overnight study between the end of their menstrual period and the time of

ovulation, the results of which have been previously reported (Ong, Taylor, et al., 2018).

Participants were compensated $200 USD for completing all study procedures.

Data Analyses

Two sets of analyses were conducted to examine group characteristics and to test the

study hypotheses. First, t-tests were conducted on self-reported measures, sleep behaviors, and

sleep parameters to examine group differences between CM and HC. The primary variables of

interest were the number of naps and mean nap duration during the study period, with $p<.025$

used as the level for statistical significance to adjust for the two comparisons. Other comparisons

on insomnia symptoms and key features of insomnia were conducted to examine sample

characteristics and clinical profiles using $p<.01$ as the level of statistical significance. Second,

hierarchical linear mixed models were implemented using PROC MIXED and PROC GLIMMIX

(SAS Institute Inc., 2013) for continuous and binary dependent variables, respectively. These

multi-level models account for the participant level dependency in the dataset, effectively

modeling the relationships between time, headache severity, and sleep behaviors and parameters

within the CM group. Participants were treated as a random effect, each receiving a random

intercept term in the models. Separate models examined the relationship between: 1) headache

severity and sleep behaviors on the same day; 2) sleep behaviors and sleep parameters on the

same day; and 3) sleep parameters and next-day headache severity. The primary sleep behavior

of interest was naps (number and duration), and the primary sleep parameter of interest was sleep

efficiency (diary and actigraphy) based on the importance of this variable as a metric for

insomnia as well as previous findings (Bertisch et al., 2020). In these analyses, $p<.0125$ was

used as the level of statistical significance to adjust for the four dependent variables.

Additionally, we explored the temporal relationship of other sleep behaviors (bed time, rise time,

TIB) that can impact sleep regulation and sleep parameters (SOL, WASO, TWT, TST) using

$p<.01$ as the level of statistical significance for these analyses. No statistical power analysis was

conducted prior to the study and the sample size was determined by the resources available from

the funding mechanism for this study.

RESULTS

Comparisons between migraine and controls

Participant characteristics are provided in Table 1. No significant differences were found

on any demographic variable.

Insomnia Symptoms. The clinical profile of self-reported measures of insomnia symptoms

and daytime functioning are presented in Table 2. The CM group scored higher than the HC

group on global measures of insomnia symptoms, including the ISI, $t(38)=6.27$, $p<.001$, and the

PSQI, $t(38)=5.91$, $p<.001$. Using validated cut-off scores for clinically significant sleep

disturbances on these measures, 13 of the 20 (65%) CM participants met the cut-off score for

poor sleepers on the PSQI (> 5) compared to none in the HC group. On the ISI, 65% (n=13) of

the CM group reported ISI ≥ 8, a cut-off score for subthreshold insomnia, and 35% (n=7)

reported ISI ≥ 15, a cut-off score for clinically significant insomnia. CM also reported more

sleep-related cognitive-emotional arousal compared to HC, including higher levels of pre-sleep

arousal as measured by the PSAS, $t(38)=4.55$, $p<.001$ and stress reactivity as measured by the

FIRST, $t(38)=4.70$, $p<.001$. On measures of daytime functioning, the CM group reported higher

levels of daytime fatigue compared to HC on the FSS, $t(38)=5.36$, $p<.001$.

Sleep behaviors. From the diary data (see Table 3), the CM group reported significantly

more days with naps (M=7.43, SD=5.66) compared to the HC group (M=3.10, SD=1.91),

$t(38)=3.23$, p=.0025. CM reported napping on 25.85% of days while the HC group napped on

9.03% of days during the study period. There were no significant differences between groups in the duration of naps, bed time, rise time, or TIB at night.

Sleep parameters. Compared to the HC group on sleep diary measures, the CM group had significantly lower SE (t[38]=4.10, p=.0003), longer SOL (t[38]=3.42, p=.0024), longer TWT (t[38]=3.51, p=.0012), and shorter TST (t[38]=3.00, p=.0047). There were no between-group differences on actigraphy measures for SE or any other sleep parameter (see Table 3).

Temporal relationships between headache severity, sleep behaviors, and sleep parameters

Headache severity and sleep behaviors. Preliminary examination of the distribution of headache severity was within normal limits for conducting linear mixed models. Within-group analyses conducted on CM examining headache severity and same-day sleep behavior (see Table 4) revealed that greater headache severity was significantly associated with longer nap duration (p=.0037). For every 1-point increase in headache severity, nap duration was 6.08 minutes longer. No other significant relationships were found.

Sleep behaviors and sleep parameters. The models examining sleep behaviors and sleep diary-measured SE on the same day (see Table 5) revealed that longer nap duration was significantly associated with lower SE (p=.0014). For each minute of nap duration, SE was .06% lower. In addition, earlier bed time (b=-.02, p=.0038), later rise time (b=.02, p=.0013), and longer time in bed (b=.02, p=.0006) were all significantly associated with higher SE measured by sleep diaries. Models examining sleep behavior and actigraphy-measured SE (see Table 5) also revealed that longer nap duration was significantly associated with lower SE (p<.0001). For each minute of nap duration, SE was .04% lower. In addition, later rise time (b=.02, p<.0001) and more time in bed (b=.02, p<.0001), were both significantly associated with higher SE.

Exploratory models examining sleep behaviors and TST on the same day revealed no significant associations between naps taken or nap duration and diary TST. Significant associations were found on bed time, rise time, and TIB for both diary and actigraphy-measured TST (see Table 6). Exploratory models examining the direct relationship between headache severity and SE found no significant associations with diary or actigraphy-measured SE. No significant associations were found on models examining sleep parameters and next-day headache severity (see Table 7).

DISCUSSION

The purpose of this study was to investigate the relationship between naps, nocturnal sleep parameters, and headache activity in CM using a micro-longitudinal design. A major strength of the study was the collection of both self-report and objective measures of sleep on a daily basis over four weeks, consistent with recommendations for assessments in behavioral clinical trials on recurrent headaches (Penzien et al., 2005). In addition, the sample was carefully screened using standardized interviews and a physical exam. The most notable finding is that napping appears to be an important sleep behavior in CM that is positively related to headache severity and can impact nocturnal sleep. Consistent with our hypothesis, we found that the frequency of naps distinguishes CM from HC. People with CM took naps on 25.85% of days compared to 11.22% of days in HC (p<.01), but the mean duration of naps in both groups was not significantly different, averaging between 80 to 90 minutes. Among those with CM, greater headache severity was significantly associated with longer nap duration, suggesting that this sleep behavior may have been used as a headache coping strategy. Furthermore, longer nap duration was significantly associated with lower SE at night, measured by both sleep diaries and

actigraphy. This finding suggests that taking longer naps could serve as an antecedent for

insomnia symptoms at night, given that low SE is characteristic of insomnia. Interestingly, SE

measured subjectively and objectively, was not associated with next-day headache severity. This

finding is similar to results from another observational study using self-reported and actigraphy-

measured sleep in tension-type headache (Kikuchi et al., 2011) but in contrast to a recent study

using similar methods in episodic migraine (Bertisch et al., 2020). Therefore, continued work is

needed to examine potential factors that might be related to the different types of headaches.

These findings indicate that napping behavior in CM merits further attention as a

potential behavioral link between migraine and insomnia. The evidence is consistent with the

hypothesis that using naps as a behavioral coping strategy for headaches during the day could be

involved in the development or maintenance of insomnia (Ong et al., 2009). In particular, longer

daytime naps can reduce the homeostatic drive for sleep at night, which can lead to lower sleep

efficiency and reduction in slow wave activity during nocturnal sleep (Lo et al., 2017). Thus,

frequently taking long naps during the day could precipitate or exacerbate insomnia symptoms,

with continued napping over time leading to chronic insomnia. As such, napping could be a

behavioral risk factor for chronic insomnia in CM, as suggested in the biobehavioral model of

headaches and insomnia (Ong & Park, 2012). A more focused model outlining the pathways

observed in this study is presented in Figure 1, which can serve as a conceptual model to be

tested in future research.

One important methodological finding was the pattern of discrepancy observed between

self-report sleep parameters from diaries and objectively-measured sleep parameters from

actigraphy. In particular, CM reported higher SOL and lower SE on sleep diaries compared to

actigraphy while HC reported lower WASO and higher SE on sleep diaries compared to

actigraphy (see Table 3). This discrepancy led to different results on some models examining

headache severity and nocturnal sleep. Given that a large portion of the literature on headache

and sleep is based upon self-report, this could explain some of the mixed findings reported in the

literature. Objective-subjective sleep discrepancy is relatively common among individuals with

insomnia disorders (Manconi et al., 2010), but self-report data are still valuable in capturing the

subjective perception of sleep (Buysse et al., 2006). Therefore, future research should consider

using both objective and self-report measures of sleep to examine potential differences between

the perception of sleep/wake patterns and actigraphy or polysomnography-measured sleep.

The findings from this study also confirm previous findings that insomnia is prominent in

people with CM. Sixty-five percent of the CM group met the cut-off scores for clinically

significant insomnia or "poor sleeper" using the ISI and PSQI respectively. Moreover, the

clinical profile of CM indicates a higher level of pre-sleep arousal, more reactivity to stress, and

more daytime fatigue when compared to HC. These clinical features are common among

individuals with primary insomnia and indicate a similar cognitive-emotional profile among

people with comorbid insomnia and CM.

The present findings should be interpreted within the limitations of the study. Although

the findings provide support for the association between headache severity, naps, and nocturnal

sleep disturbance, it does not establish causality since this was not an experimental design. Given

that nap data were self-reported and not objectively measured, the actual amount of sleep that

occurred during naps could not be determined. Furthermore, the specific timing of naps and the

reason for taking naps were not systematically evaluated in this study. Therefore, the present

findings cannot rule out that CM sufferers were resting rather than actually sleeping during naps,

that there were other potential reasons why they were taking naps, or that there were other

potential causes of nocturnal sleep disturbance. In addition, the timeframe we examined focused on the same day and next day effects which do not rule out delayed effects (e.g., let down headache) that might have a longer temporal association (Houle, Penzien, & Rains, 2005). Also, the present study only recruited women and therefore further studies examining men with migraine are needed. Finally, the sample size had limited power to adjust for potential confounders or to conduct moderation analyses on insomnia status.

Despite these limitations, the findings provide important new data on the potential impact of napping behavior as a possible link between migraine headaches and insomnia. Given the preliminary nature of these findings, future studies should employ rigorous designs to confirm these findings or test competing hypotheses. For example, elucidating the actual duration of sleep during naps along with the timing of naps and its impact on nocturnal sleep and headache activity could address some limitations of the present study. Similarly, clarifying the nature of sleep disturbance with regards to sleep duration and sleep microarchitecture is needed. Future research should also examine if napping behaviors change over the course of insomnia to determine if it is a precipitating or perpetuating factor.

Should these findings be confirmed, they could have clinical implications with regards to using cognitive-behavior therapy for insomnia (CBT-I) in people with migraine. Given that the cognitive component of CBT-I is designed to address sleep-related arousal, the present findings lend further support for using CBT-I in people with CM, which has promising indications for effectiveness (Crawford et al., 2020; Smitherman et al., 2016). Clinicians who deliver CBT-I might also need to pay particular attention to napping behavior and be prepared to discuss alternative coping strategies for managing acute headache pain during the day, such as mindfulness meditation, which can shift pain appraisal and reduce negative arousal without

disturbing sleep at night (Ong et al., 2014; Ong, Xia, Smith-Mason, & Manber, 2018; Wells et

al., 2020).

Conflict of Interest Disclosures: Jason Ong is employed by Nox Health, Inc and has served as a consultant to Headspace, Inc, Vox Media, LLC, and Weight Watchers International, Inc. These activities are not related to this study. Spencer Dawson serves on the advisory board of Better Sleep. This activity is not related to this study. Todd A. Smitherman serves on an advisory board for Teva. This activity is unrelated to this study. Helen Burgess is a consultant for Natrol, LLC. This activity is not related to this study. Colin Espie is a Co-founder of and a shareholder in Big Health Inc, which developed and maintained the sleep diaries used in this study. All other authors report no conflict.

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Table 1. Participant Characteristics.

	CM (n=20)	HC (n=20)
Age, years		
mean (SD)	32.67 (5.82)	32.20 (6.17)
Ethnicity (% Hispanic)	10%	5%
Race (%)		
White	55%	70%
Black	25%	25%
More than 1 race	15%	5%
American Indian	5%	0%
Years of Education		
Mean (SD)	15.75 (3.67)	17.06 (2.18)
Relationship Status (%)		
Partnered	65%	60%
Single	30%	40%
Divorced/Separated	5%	0%
Employment (%)		
Full-Time	65%	65%
Part-Time	10%	5%
Unemployed	5%	5%
Caregiver	10%	15%
Student	10%	10%
Medications (n)		
OTC analgesics	9	0
NSAIDs	7	4
Triptans	9	0
Antihistamines	7	3
Antidepressants	6	0
Opiates	4	0
Benzodiazepines/Hypnotics	4	0
Antihypertensives	3	0
Antiepileptics	2	0
Headache days per month (mean, SD)		
Migraine	18.0 (6.2)	N/A
Other headaches types	5.9 (8.2)	0.5 (0.5)

Note. CM = Chronic Migraine; HC = Healthy Control; SD = Standard Deviation

Table 2. Self-Report Questionnaires

	CM Mean (SD)	HC Mean (SD)	*p*
PSQI	8.00 (5.01)	1.30 (0.80)	<.001*
ISI	10.70 (6.84)	0.95 (1.23)	<.001*
PSAS	31.35 (12.51)	18.40 (2.37)	<.001*
FIRST	21.40 (5.90)	14.00 (3.85)	<.001*
HAS	61.35 (9.87)	55.25 (9.85)	.058
DBAS	106.20 (31.35)	84.35 (34.27)	.042
FSS	36.20 (13.41)	18.15 (6.83)	<.001*
ESS	7.75 (5.78)	4.20 (2.48)	.016

* p<.01

Note. CM = Chronic Migraine; HC = Healthy Control; SD = Standard Deviation; PSQI = Pittsburgh Sleep Quality Index; ISI = Insomnia Severity Index; PSAS = Pre-Sleep Arousal Scale; FIRST = Ford Insomnia Response to Stress Test; HAS = Hyperarousal Scale; DBAS = Dysfunctional Beliefs and Attitudes about Sleep; FSS = Fatigue Severity Scale; ESS = Epworth Sleepiness Scale

Table 3. Sleep Behaviors and Sleep Parameters.

	CM		HC			
	Mean (SD)	Range	Mean (SD)	Range	t	p
Sleep Behavior						
Days with naps	7.43 (5.66)	0-23	3.10 (1.91)	0-8	-3.23	0.0025*
% of days with naps	25.85 (20.34)	0-85.19	11.22 (7.09)	0-28.57	3.04	0.0043
Nap duration (min)	88.72 (49.03)	8.75-208.7	80.20 (61.15)	11.67-228	-0.47	0.6441
Bed Time (hour:min)	23:25 (1:04)	21:08-1:09	23:47 (1:14)	22:01-2:45	1.02	0.3159
Rise Time (hour:min)	7:27 (1:08)	5:49-9:38	7:48 (1:00)	5:58-9:52	1.07	0.2897
TIB (min)	501.04 (56.34)	388.06-598.89	491.28 (42.14)	400.18-568.89	-0.62	0.5385
Diary-Based Sleep Data						
SOL (min)	29.11 (23.63)	6.00-112.04	10.15 (7.49)	0.91-33.00	-3.42	0.0024*
WASO (min)	28.12 (31.09)	3.39-132.78	12.70 (11.89)	1.25-44.58	-2.07	0.0489*
TWT (min)	57.23 (41.37)	10.48-181.5	22.85 (14.25)	6.96-52.22	-3.51	0.0012*
SE (%)	80.39 (10.01)	57.48-94.54	90.98 (5.76)	80.63-98.46	4.10	0.0003*
TST (min)	402.74 (47.58)	310.41-484.29	446.91 (45.39)	337.68-534.52	3.00	0.0047*
Actigraphy-Based Sleep Data						
SOL (min)	14.03 (11.02)	2.57-44.75	13.60 (12.48)	2.07-55.94	-0.12	0.9084
WASO (min)	37.39 (13.37)	19.48-73.52	39.57 (14.20)	12.36-71.46	0.50	0.6201
TWT (min)	65.45 (25.27)	36.90-136.6	70.35 (24.80)	31.86-134.8	0.62	0.5397
SE (%)	86.20 (5.06)	71.52-92.64	85.22 (4.75)	74.16-93.19	-0.63	0.5320
TST (min)	412.55 (40.55)	337.77-468.68	409.94 (34.45)	325.41-470.59	-0.22	0.8272

* p<.025 for days with naps; * p < .01 for Diary-Based SOL, WASO, TWT, SE, TST

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Note. CM = Chronic Migraine; HC = Healthy Control; SD = Standard Deviation; TIB = Time in Bed; SOL = Sleep Onset Latency; WASO = Wake after Sleep Onset; TWT = Total Wake Time; SE = Sleep Efficiency; TST = Total Sleep Time

Table 4. Headache Severity Predicting Same Day Sleep Behavior

Independent Variable	Dependent Variable	b	SE	95% CI	t	p
Headache Severity	Nap (yes/no)	0.07	0.04	-0.01, 0.14	1.79	0.0735
Headache Severity	Nap duration (min)	6.08	2.05	2.01, 10.14	2.96	0.0037*
Headache Severity	Bed Time (min from midnight)	-2.62	1.10	-4.78, -0.48	-2.39	0.0171
Headache Severity	Rise Time (min from midnight)	-0.30	1.21	-2.68, 2.08	-0.25	0.8057
Headache Severity	Time in Bed (min)	2.02	1.35	-0.63, 4.66	1.5	0.1344

* $p < .0125$ for Nap duration

Note. Headache severity was measured on a 0-10 scale indicating maximum headache severity. The nap variable was a dichotomous variable based on whether a nap was reported the same day as the headache severity rating. Nap duration was the mean duration of the nap on days when a nap was taken. Units for bed time and rise time are reported in minutes centered on midnight, such that negative values are before midnight and positive values are after midnight.

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Table 5. Sleep Behavior Predicting Same Night Sleep Efficiency

Independent Variable	Dependent Variable	b	SE	95% CI	t	p
Nap (yes/no)	Diary Sleep Efficiency (%)	-0.51	1.43	-3.31, 2.29	-0.36	0.7210
Nap duration (min)	Diary Sleep Efficiency (%)	-0.06	0.02	-0.10, -0.02	-3.27	0.0014*
Bed Time (min from midnight)	Diary Sleep Efficiency (%)	-0.02	0.01	-0.04, -0.01	-2.90	0.0038*
Rise Time (min from midnight)	Diary Sleep Efficiency (%)	0.02	0.01	0.01, 0.04	3.24	0.0013*
Time in Bed (min)	Diary Sleep Efficiency (%)	0.02	0.01	0.01, 0.03	3.44	0.0006*
Nap (yes/no)	Actigraphy Sleep Efficiency (%)	-0.87	0.83	-2.49, 0.76	-1.05	0.2951
Nap duration (min)	Actigraphy Sleep Efficiency (%)	-0.04	0.01	-0.06, -0.02	-4.41	<.0001*
Bed Time (min from midnight)	Actigraphy Sleep Efficiency (%)	-0.004	0.005	-0.01, 0.01	-0.83	0.4066
Rise Time (min from midnight)	Actigraphy Sleep Efficiency (%)	0.023	0.004	0.01, 0.03	5.57	<.0001*
Time in Bed (min)	Actigraphy Sleep Efficiency (%)	0.02	0.00	0.01, 0.03	5.88	<.0001*

* p<.0125 for Nap duration
* p<.01 for Bed Time, Rise Time, and Time in Bed

Note. The nap variable was a dichotomous variable based on whether a nap was reported on that day. Nap duration was the mean duration of the nap on days when a nap was taken. Units for bed time and rise time are reported in minutes centered on midnight, such that negative values are before midnight and positive values are after midnight.

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Table 6. Sleep Behavior Predicting Same Night Total Sleep Time

Independent Variable	Dependent Variable	b	SE	95% CI	t	p
Nap (yes/no)	Diary TST (min)	-5.64	10.63	-26.52, 15.25	-0.53	0.5963
Nap duration (min)	Diary TST (min)	-0.21	0.14	-0.48, 0.06	-1.52	0.1319
Bed Time (min from midnight)	Diary TST (min)	-0.57	0.05	-0.67, -0.46	-10.53	<.0001*
Rise Time (min from midnight)	Diary TST (min)	0.67	0.05	0.58, 0.76	14.51	<.0001*
Time in Bed (min)	Diary TST (min)	0.91	0.03	0.85, 0.97	29.71	<.0001*
Nap (yes/no)	Actigraphy TST (min)	-8.57	9.21	-26.66, 9.52	-0.93	0.3523
Nap duration (min)	Actigraphy TST (min)	-0.25	0.13	-0.51, 0.01	-1.89	0.0613
Bed Time (min from midnight)	Actigraphy TST (min)	-0.48	0.05	-0.58, -0.39	-10.31	<.0001*
Rise Time (min from midnight)	Actigraphy TST (min)	0.60	0.04	0.52, 0.67	15.19	<.0001*
Time in Bed (min)	Actigraphy TST (min)	0.79	0.03	0.74, 0.84	31.17	<.0001*

* p<.01 for Bed Time, Rise Time, and Time in Bed

Note. Headache severity was measured on a 0-10 scale indicating maximum headache severity. The nap variable was a dichotomous variable based on whether a nap was reported. Nap duration was the mean duration of the nap on days when a nap was taken. TST = Total Sleep Time. Units for bed time and rise time are reported in minutes centered on midnight, such that negative values are before midnight and positive values are after midnight.

Table 7. Sleep Predicting Next Day Headache Severity

Independent Variable	Dependent Variable	b	Std Err	95% CI	t	p
Diary TST (min)	Next Day Headache Severity	-0.13	0.07	-0.27, 0.00	-1.96	0.0505
Actigraphy TST (min)	Next Day Headache Severity	-0.11	0.08	-0.27, 0.05	-1.33	0.1843
Diary SE (%)	Next Day Headache Severity	-0.01	0.01	-0.03, 0.01	-0.99	0.3228
Actigraphy SE (%)	Next Day Headache Severity	-0.01	0.02	-0.04, 0.02	-0.92	0.3562

Note. TST = Total Sleep Time; SE = Sleep Efficiency; Std Err = Standard Error. Headache severity was measured on a 0-10 scale indicating maximum headache severity.

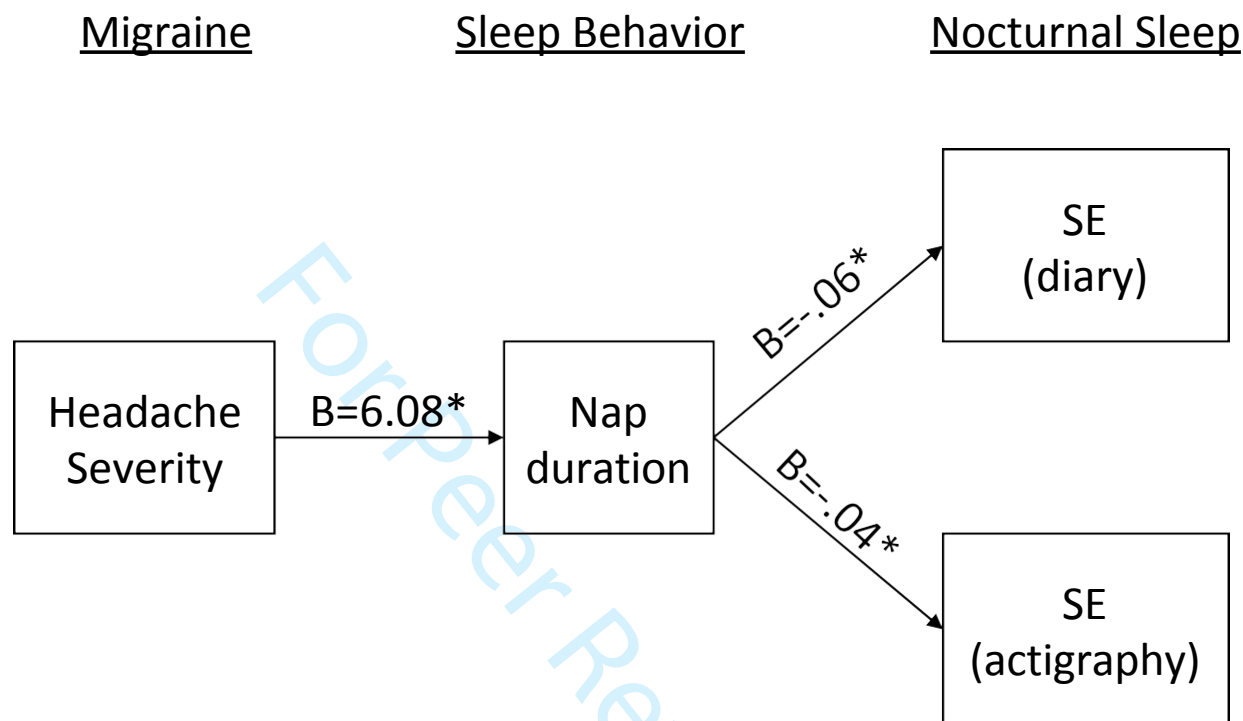Figure 1. Hypothesized model and significant observed relationships

Figure 1 Caption.

This figure depicts a proposed temporal pathway based on the findings from this study. In this model, migraine headache severity is associated with nap duration as a sleep behavior, which leads to decreased sleep efficiency (SE) at night, as measured by both self-reported diaries and actigraphy. B = beta weights; * p<.0125

Supplement 2. Protocol for Actigraphy Scoring

The following protocol was used for scoring rest periods at night to determine sleep and wake parameters, including SOL, WASO, TWT, TST, SE. Data were analyzed in 60 second epochs using medium sensitivity for determining wakefulness with Respironics Actiware version 6.0.

 When both diary and event markers were available and within 60 minutes of one another, the event marker was used; if the discrepancy was greater than 60 minutes and the event marker was within 60 minutes of an observable change in activity, then the event marker was used; if neither sleep diary nor observable change in activity was within 60 minutes of the event marker, then the bed time/rise time determined by the actigraphy software program was used. If there was no event marker and there was a change in activity observed within 60 minutes, then the diary was used; if not then the algorithm was used. If neither event marker nor sleep diary were available to determine bed or wake time, then that night was treated as missing. Similarly, if the off-wrist detection indicated the participant was not wearing the device, the night was treated as missing.

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A Micro-Longitudinal Study of Naps, Sleep Disturbance, and Headache Severity in Women

with Chronic Migraine

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ABSTRACT

Objective: To examine the relationship between headaches, naps, and nocturnal sleep in women

with chronic migraine (CM) using micro-longitudinal data from diaries and actigraphy.

Methods: 20 women with CM and 20 age and sex-matched healthy controls (HC) completed

self-report questionnaires, electronic diaries, and wrist actigraphy over a 4-week period.

Between-group comparisons were conducted with naps (frequency and duration) as the primary

variable of interest. Within-group analyses were conducted on the CM group using hierarchical

linear mixed models to examine the temporal relationships between headache severity, sleep

behaviors, and sleep parameters. The primary variables of interest were naps (number and

duration) and nocturnal sleep efficiency (diary and actigraphy).

Results: The CM group reported significantly more days with naps (25.85%) compared to the

HC group (9.03%) during the study period (p=.0025). Within-group analyses in CM revealed

that greater headache severity was associated with longer nap duration (p=.0037) and longer nap

duration was associated with lower sleep efficiency measured using diaries (p=.0014) and

actigraphy (p<.0001).

Conclusions: Napping is more frequent in CM than HC and nap duration in CM is associated

with headache severity and nocturnal sleep disturbance. These findings provide initial support

for the hypothesis that daytime napping is a behavioral coping strategy used in CM that could

contribute to insomnia.

Key Words: migraine, sleep, insomnia, naps, actigraphy, women

INTRODUCTION

Sleep disturbance is prominent in chronic migraine (CM) and is implicated as a risk factor in headache exacerbation. Poor sleep has been found to precede migraine headaches (Andress-Rothrock, King, & Rothrock, 2010; Boardman, Thomas, Millson, & Croft, 2006; Kelman & Rains, 2005; Odegard et al., 2011; Pellegrino, Davis-Martin, Houle, Turner, & Smitherman, 2018) but other studies have found inconsistent or contrary results (Bertisch et al., 2020; Blau, 1982; Kikuchi, Yoshiuchi, Yamamoto, Komaki, & Akabayashi, 2011). Findings are further limited by methodological issues including reliance on self-report measures and inconsistencies in characterizing the type of sleep disturbance (for a critical review see (Ong & Park, 2012). As a result, the relationship between sleep and migraine remains complicated and unclear and new approaches are needed.

Compared to nocturnal sleep, daytime naps have been relatively understudied in migraine. Naps are often used as a behavioral coping strategy for headaches (Haque et al., 2012; Ong, Stepanski, & Gramling, 2009), but models of insomnia have demonstrated that daytime naps can contribute to the development and maintenance of insomnia (Spielman, Caruso, & Glovinsky, 1987). It has been posited that people with CM who frequently take naps as a headache-coping strategy could be at risk for developing a comorbid insomnia disorder (Ong & Park, 2012). To our knowledge, the impact of daytime naps on nighttime sleep and next-day headaches has not been specifically examined in CM.

The purpose of this study was to examine the relationship between headaches, sleep behaviors, and sleep parameters in women with CM using micro-longitudinal data from diaries and wrist actigraphy. This study focused on women because the rate of migraine is three to four times higher compared to men and the one-year prevalence of migraine attacks in men is only

6% (Al-Hassany et al., 2020) and . Furthermore, women are at higher risk for insomnia than men (Ohayon, 2002). The goal was to explore the hypothesis that napping is a common behavior in CM that is associated with nocturnal sleep disturbance and could play an important role in the link between headaches and insomnia. Specifically, we hypothesized that: 1) women with CM take more frequent naps than matched healthy controls, 2) napping in CM is temporally associated with more sleep disturbance at night as indicated by lower sleep efficiency, and 3) lower sleep efficiency in CM is temporally associated with next-day headache severity. In addition to these main hypotheses, we explored the relationship among headache severity, sleep, and other sleep behaviors relevant to insomnia.

METHODS

Participants

Participants were 40 females between the ages of 18 and 40 without signs of perimenopause. Participants were primarily recruited from the community through posted advertisements, flyers, and emails sent to a women's health registry list. Eligibility screening consisted of a telephone interview followed by an in-person interview that included a review of medical history, structured diagnostic interviews for headache (Andrew, Penzien, Rains, Knowlton, & McAnulty, 1992), sleep disorders (Edinger et al., 2011), and psychiatric conditions (First, 1995). Diagnosis of migraine was confirmed by review of symptoms and a medical exam with the study neurologist.

Women in the CM group met the International Classification of Headache (3rd edition) for CM (2018). Participants with CM were age-matched (+/- 3 years) to a participant in the healthy control group. Those in the healthy control (HC) group who had no history of headache

disorder and ≤ 1 headache day per month in the past 12 months. Exclusion criteria for both

groups included unstable medical or psychiatric conditions that would interfere with the study

protocol or require immediate treatment, regular use of illegal substances or medications known

to affect sleep or melatonin, pregnancy or nursing, engagement in night shift work, and travel

across more than three time zones in the month prior to enrollment (see supplement 21 for

details). The study was approved by the Institutional Review Board at Rush University Medical

Center and all participants provided written informed consent prior to participation.

Measures

Self-Report Questionnaires

Several self-reported measures commonly used in the clinical assessment of migraine or

sleep disorders were collected to evaluate the clinical profile of the sample. The Pittsburgh Sleep

Quality Index (PSQI) (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) and Insomnia

Severity Index (ISI) (Bastien, Vallieres, & Morin, 2001) are standard measures that assess global

symptoms of sleep disturbances and daytime dysfunction related to sleep and include validated

cut-offs for clinically significant symptoms of insomnia. The Pre-Sleep Arousal Scale (PSAS)

(Nicassio, Mendlowitz, Fussell, & Petras, 1985), Hyperarousal Scale (Pavlova et al., 2001),

Dysfunctional Beliefs and Attitudes about Sleep (DBAS) (Morin, Stone, Trinkle, Mercer, &

Remsberg, 1993), and Ford Insomnia Response to Stress Test (FIRST) (Drake, Richardson,

Roehrs, Scofield, & Roth, 2004) were used to assess cognitive and emotional factors related to

insomnia. The Fatigue Severity Scale (FSS) (Krupp, LaRocca, Muir-Nash, & Steinberg, 1989)

and Epworth Sleepiness Scale (ESS) (Johns, 1991) were used to assess the associated daytime

impairment related to sleep disturbances. In addition to these measures, demographic data and

the number of migraine days per month (30 days) were collected during the screening visit.

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Sleep and Headache Diaries

Prospective daily diaries were used to measure self-reported sleep and headache activity

throughout the study duration via a secure website designed for this study. For sleep behaviors,

participants were asked about the following items: the time of getting into bed at night, bed time

(time intending to go to sleep), rise time (time getting out of bed in the morning), and the number

and duration of naps during the day. For sleep parameters, participants were asked to report sleep

onset latency (SOL), wake after sleep onset (WASO), and total sleep time (TST). Time in bed

(TIB; calculated as the duration from bed time to rise time), total wake time (TWT; calculated as

SOL + WASO), total sleep time (TST; calculated as TIB minus TWT), and sleep efficiency (SE

= TST/TIB x 100) were derived from these sleep parameters. The sleep items follow the

recommendations for a standardized sleep diary (Carney et al., 2012) and are considered to be

the standard of practice for self-reported measurement of sleep/wake patterns (Buysse, Ancoli-

Israel, Edinger, Lichstein, & Morin, 2006). Maximum headache severity was assessed each day

on a 0-10 scale (0=no headache, 10=most severe headache). Participants were asked to complete

each diary entry within one hour of their rise time based on the activities of the previous

day. Each entry was time-stamped and reviewed by the research team to minimize recall bias. To

minimize missing data, participant compensation was reduced if they missed more than two days

of diary entries.

Actigraphy

Wrist actigraphy (Actiwatch Spectrum, Phillips Respironics, Bend, OR) was used to measure

objective sleep/wake patterns concurrent with the sleep diaries throughout the study period.

Actigraphy is commonly used to assess longitudinal sleep/wake patterns and has been well-validated as an objective measure of sleep (Buysse et al., 2006). Participants were instructed to wear the actigraph on the non-dominant hand during the day and night, using the event marker on the device to indicate bed time and rise time. Rest intervals were manually set according to a pre-established protocol used in previous studies (see supplement 12 for details) (Ong et al., 2014; Ong, Taylor, et al., 2018). Data were analyzed in 60 second epochs using medium sensitivity for determining wakefulness with Respironics Actiware version 6.0.

Procedure

The present study is an observational, micro-longitudinal study examining the self-reported diaries and actigraphy data collected as part of a previously published study (Ong, Taylor, et al., 2018). A total of 65 potential participants were screened for eligibility with 24 CM and 20 HC qualifying the study. Two CM participants did not complete the assessment protocol and two other CM participants were unmatched, resulting in the final sample size of 20 CM and 20 HC.

The study duration (mean = 28.20 days, SD = 3.16 days, range = 21-36 days) was selected to include one complete menstrual cycle or 28 days for women who did not have a regular menstrual cycle (i.e., due to IUD, continuous hormonal birth control, or hysterectomy). The number of days observed was not significantly different between the CM (M=28.20, SD=3.44) and HC (M=27.55, SD=2.80) groups. Following a brief orientation upon determining eligibility, participants were provided with instructions for the at-home monitoring protocol, which included tracking of sleep and headache data how to use the using an actigraph and the online sleep/headache diary, beginning on day 1 of their menstrual cycle and continuing until the start of the next menstrual cycle. Participants completed an in-lab overnight study between the end of their menstrual period and the time of ovulation, the results of which have been

previously reported (Ong, Taylor, et al., 2018). Participants were compensated $200 USD for

completing all study procedures.

Data Analyses

Two sets of analyses were conducted to examine group characteristics and to test the

study hypotheses. First, t-tests were conducted on self-reported measures, sleep behaviors, and

sleep parameters to examine group differences between CM and HC. The primary variables of

interest were the number of naps and mean nap duration during the study period, with $p<.025$

used as the level for statistical significance to adjust for the two comparisons. Other comparisons

on insomnia symptoms and key features of insomnia were conducted to examine sample

characteristics and clinical profiles using $p<.01$ as the level of statistical significance. Second,

hierarchical linear mixed models were implemented using PROC MIXED and PROC GLIMMIX

(SAS Institute Inc., 2013) for continuous and binary dependent variables, respectively. These

multi-level models ~~allow us to~~ account for the participant level dependency in the dataset,

effectively modeling the relationships between time, headache severity, and sleep behaviors and

parameters within the CM group. Participants were treated as a random effect, each receiving a

random intercept term in the models. Separate models examined the relationship between: 1)

headache severity and sleep behaviors on the same day; 2) sleep behaviors and sleep parameters

on the same day; and 3) sleep parameters and next-day headache severity. The primary sleep

behavior of interest was naps (number and duration), and the primary sleep parameter of interest

was sleep efficiency (diary and actigraphy) based on <u>the importance of this variable as a metric

for insomnia as well as</u> previous findings (Bertisch et al., 2020). In these analyses, $p<.0125$ was

used as the level of statistical significance to adjust for the four dependent variables.

Additionally, we explored the temporal relationship of other sleep behaviors (bed time, rise time,

TIB) that can impact ~~are of importance to~~ sleep regulation and sleep parameters (SOL, WASO, TWT, TST) ~~that are commonly measured in sleep medicine and research~~ using *p*<.01 as the level of statistical significance for these analyses. No statistical power analysis was conducted prior to the study and the sample size was determined by the resources available from the funding mechanism for this study.

RESULTS

Comparisons between migraine and controls

Participant characteristics are provided in Table 1. No significant differences were found on any demographic variable.

Insomnia Symptoms. The ~~o examine the~~ clinical profile ~~features~~ of ~~insomnia, we compared CM and HC on~~ self-reported measures of insomnia symptoms and daytime functioning are presented in ~~(see~~ Table 2~~)~~. The CM group scored higher than the HC group on global measures of insomnia symptoms, including the ISI, t(38)=6.27, p<.001, and the PSQI, t(38)=5.91, p<.001. Using validated cut-off scores for clinically significant sleep disturbances on these measures, 13 of the 20 (65%) CM participants met the cut-off score for poor sleepers on the PSQI (> 5) compared to none in the HC group. On the ISI, 65% (n=13) of the CM group reported ISI ≥ 8, a cut-off score for subthreshold insomnia, and 35% (n=7) reported ISI ≥ 15, a cut-off score for clinically significant insomnia. CM also reported more sleep-related cognitive-emotional arousal compared to HC, including higher levels of pre-sleep arousal as measured by the PSAS, t(38)=4.55, *p*<.001 and stress reactivity as measured by the FIRST, t(38)=4.70, *p*<.001. On measures of daytime functioning, the CM group reported higher levels of daytime fatigue compared to HC on the FSS, t(38)=5.36, p<.001.

Sleep behaviors. From the diary data (see Table 3), the CM group reported significantly more days with naps (M=7.43, SD=5.66) compared to the HC group (M=3.10, SD=1.91), t(38)=3.23, p=.0025. CM reported napping on 25.85% of days while the HC group napped on 9.03% of days during the study period. There were no significant differences between groups in the duration of naps, bed time, rise time, or TIB at night.

Sleep parameters. Compared to the HC group on sleep diary measures, the CM group had significantly lower SE (t[38]=4.10, p=.0003), longer SOL (t[38]=3.42, p=.0024), longer TWT (t[38]=3.51, p=.0012), and shorter TST (t[38]=3.00, p=.0047). There were no between-group differences on actigraphy measures for SE or any other sleep parameter (. Ssee Table 3) for means and standard deviations.

Temporal relationships between headache severity, sleep behaviors, and sleep parameters

Headache severity and sleep behaviors. Preliminary examination of the distribution of headache severity was within normal limits for conducting linear mixed models. Within-group analyses conducted on CM examining headache severity and same-day sleep behavior (see Table 4) revealed that greater headache severity was significantly associated with longer nap duration (p=.0037). For every 1-point increase in headache severity, nap duration was 6.08 minutes longer. No other significant relationships were found.

Sleep behaviors and sleep parameters. The models examining sleep behaviors and sleep diary-measured SE on the same day (see Table 5) revealed that longer nap duration was significantly associated with lower SE (p=.0014). For each minute of nap duration, SE was .06% lower. In addition, earlier bed time (b=-32.98.02, p=.0038), later rise time (b=33.50.02, p=.0013), and longer time in bed (b=.02, p=.0006) were all significantly associated with higher

SE measured by sleep diaries. Models examining sleep behavior and actigraphy-measured SE (see Table 5) also revealed that longer nap duration was significantly associated with lower SE (p<.0001). For each minute of nap duration, SE was .04% lower. In addition, later rise time (b=.0232.68, p<.0001) and more time in bed (b=.02, p<.0001), were both significantly associated with higher SE.

Exploratory models examining sleep behaviors and TST on the same day revealed no significant associations between naps taken or nap duration and diary TST. Significant associations were found on bed time, rise time, and TIB for both diary and actigraphy-measured TST (. Ssee Table 6 for details). Exploratory models examining the direct relationship between headache severity and SE found no significant associations with diary or actigraphy-measured SE. No significant associations were found on models examining sleep parameters and next-day headache severity (see Table 7).

DISCUSSION

The purpose of this study was to investigate the relationship between naps, nocturnal sleep parameters, and headache activity in CM using a micro-longitudinal design. A major strength of the study was the collection of both self-report and objective measures of sleep on a daily basis over four weeks, consistent with recommendations for assessments in behavioral clinical trials on recurrent headaches (Penzien et al., 2005). In addition, the sample was carefully screened using standardized interviews and a physical exam. The most notable finding is that napping appears to be an important sleep behavior in CM that is positively related to headache severity and can impact nocturnal sleep. Consistent with our hypothesis, we found that the frequency of naps distinguishes CM from HC. People with CM took naps on 25.85% of days

compared to 11.22% of days in HC (p<.01), but the mean duration of naps in both groups was not significantly different, averaging between 80 to 90 minutes. Among those with CM, greater headache severity was significantly associated with longer nap duration, suggesting that this sleep behavior may have been used as a headache coping strategy. Furthermore, longer nap duration was significantly associated with lower SE at night, measured by both sleep diaries and actigraphy. This finding suggests that taking longer naps could serve as an antecedent for insomnia symptoms at night, given that low SE is characteristic of insomnia. Interestingly, SE measured subjectively and objectively, was not associated with next-day headache severity. This finding is similar to results from another observational study using self-reported and actigraphy-measured sleep in tension-type headache (Kikuchi et al., 2011) but in contrast to a recent study using similar methods in episodic migraine (Bertisch et al., 2020). Therefore, continued work is needed to examine potential factors that might be related to the different types of headaches.

These findings indicate that napping behavior in CM merits further attention as a potential behavioral link between migraine and insomnia. The evidence is consistent with the hypothesis that using naps as a behavioral coping strategy for headaches during the day could be involved in the development or maintenance of insomniais an antecedent for lower objective sleep efficiency at night (Ong et al., 2009). In particular, longer daytime naps can reduce the homeostatic drive for sleep at night, which can lead to lower sleep efficiency and reduction in slow wave activity during nocturnal sleep (Lo et al., 2017). Thus, frequently taking long naps during the day could precipitate or exacerbate insomnia symptoms, with continued napping over time leading to chronic insomnia. As such, napping could be a behavioral risk factor for chronic insomnia in CM, as suggested in the biobehavioral model of headaches and insomnia (Ong &

Park, 2012). A more focused model outlining the pathways observed in this study is presented in

Figure 1, which can serve as a conceptual model to be tested in future research.

One important methodological finding was the pattern of discrepancy observed between

self-report sleep parameters from diaries and objectively-measured sleep parameters from

actigraphy. In particular, CM reported higher SOL and lower SE on sleep diaries compared to

actigraphy while HC reported lower WASO and higher SE on sleep diaries compared to

actigraphy (see Table 3). This discrepancy led to different results on some models examining

headache severity and nocturnal sleep. Given that a large portion of the literature on headache

and sleep is based upon self-report, this could explain some of the mixed findings reported in the

literature. Objective-subjective sleep discrepancy is relatively common among individuals with

insomnia disorders (Manconi et al., 2010), but self-report data are still valuable in capturing the

subjective perception of sleep (Buysse et al., 2006). Therefore, future research should consider

using both objective and self-report measures of sleep to examine potential differences between

the perception of sleep/wake patterns and actigraphy or polysomnography-measured sleep.

The findings from this study also confirm previous findings that insomnia is prominent in

people with CM. Sixty-five percent of the CM group met the cut-off scores for clinically

significant insomnia or "poor sleeper" using the ISI and PSQI respectively. Moreover, the

clinical profile of CM indicates a higher level of pre-sleep arousal, more reactivity to stress, and

more daytime fatigue when compared to HC. These clinical features are common among

individuals with primary insomnia and indicate a similar cognitive-emotional profile among

people with comorbid insomnia and CM.

The present findings should be interpreted within the limitations of the study. Although

the findings provide support for the association between headache severity, naps, and nocturnal

sleep disturbance, it does not establish causality since this was not an experimental design. Given that nap data were self-reported and not objectively measured, the actual amount of sleep that occurred during naps could not be determined. Furthermore, the specific timing of naps and the reason for taking naps were not systematically evaluated in this study. Therefore, the present findings cannot rule out that CM sufferers were resting rather than actually sleeping during naps, that there were other potential reasons why they were taking naps, or that there were other potential causes of nocturnal sleep disturbance. In addition, the timeframe we examined focused on the same day and next day effects which do not rule out delayed effects (e.g., let down headache) that might have a longer temporal association (Houle, Penzien, & Rains, 2005). Also, the present study only recruited women and therefore further studies examining men with migraine are needed. Finally, the sample size had limited power to adjust for potential confounders or to conduct moderation analyses on insomnia status.was relatively small and could be underpowered to detect between-group effects.

Despite these limitations, the findings provide important new data on the potential impact of napping behavior as a possible link between migraine headaches and insomnia. Given the preliminary nature of these findings, future studies should employ rigorous designs to confirm these findings or test competing hypotheses. For example, can build upon these findings by elucidating the actual duration of sleep during naps along with the timing of naps and its impact on nocturnal sleep and headache activity could address some limitations of the present study. Similarly, clarifying the nature of sleep disturbance with regards to sleep duration and sleep microarchitecture is needed. Future research should also examine if napping behaviors change over the course of insomnia to determine if it is a precipitating or perpetuating risk factor.

Should these The findings be confirmed, they also have could have clinical implications

with regards to using cognitive-behavior therapy for insomnia (CBT-I) in people with migraine.

Given that the cognitive component of CBT-I is designed to address sleep-related arousal, the

present findings lend further support for using CBT-I in people with CM, which has promising

indications for effectiveness (Crawford et al., 2020; Smitherman et al., 2016). Clinicians who

deliver CBT-I might also need to pay particular attention to napping behavior and be prepared to

discuss alternative coping strategies for managing acute headache pain during the day, such as .

Future studies can provide further guidance to clinicians by examining strategies to reduce naps

or using alternative coping strategies such as mindfulness meditation, which can shift pain

appraisal and reduce negative arousal without disturbing sleep at night (Ong et al., 2014; Ong,

Xia, Smith-Mason, & Manber, 2018; Wells et al., 2020).

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Table 1. Participant Characteristics.

	CM (n=20)	HC (n=20)
Age, years		
mean (SD)	32.67 (5.82)	32.20 (6.17)
Ethnicity (% Hispanic)	10%	5%
Race (%)		
White	55%	70%
Black	25%	25%
More than 1 race	15%	5%
American Indian	5%	0%
Years of Education		
Mean (SD)	15.75 (3.67)	17.06 (2.18)
Relationship Status (%)		
Partnered	65%	60%
Single	30%	40%
Divorced/Separated	5%	0%
Employment (%)		
Full-Time	65%	65%
Part-Time	10%	5%
Unemployed	5%	5%
Caregiver	10%	15%
Student	10%	10%
Medications (n)		
OTC analgesics	9	0
NSAIDs	7	4
Triptans	9	0
Antihistamines	7	3
Antidepressants	6	0
Opiates	4	0
Benzodiazepines/Hypnotics	4	0
Antihypertensives	3	0
Antiepileptics	2	0
Headache days per month (mean, SD)		
Migraine	18.0 (6.2)	N/A
Other headaches types	5.9 (8.2)	0.5 (0.5)

Note. CM = Chronic Migraine; HC = Healthy Control; SD = Standard Deviation

MIGRAINE AND SLEEP

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Table 2. Self-Report Questionnaires

	CM Mean (SD)	HC Mean (SD)	*p*
PSQI	8.00 (5.01)	1.30 (0.80)	<.001*
ISI	10.70 (6.84)	0.95 (1.23)	<.001*
PSAS	31.35 (12.51)	18.40 (2.37)	<.001*
FIRST	21.40 (5.90)	14.00 (3.85)	<.001*
HAS	61.35 (9.87)	55.25 (9.85)	.058
DBAS	106.20 (31.35)	84.35 (34.27)	.042
FSS	36.20 (13.41)	18.15 (6.83)	<.001*
ESS	7.75 (5.78)	4.20 (2.48)	.016

* p<.01

Note. CM = Chronic Migraine; HC = Healthy Control; SD = Standard Deviation; PSQI = Pittsburgh Sleep Quality Index; ISI = Insomnia Severity Index; PSAS = Pre-Sleep Arousal Scale; FIRST = Ford Insomnia Response to Stress Test; HAS = Hyperarousal Scale; DBAS = Dysfunctional Beliefs and Attitudes about Sleep; FSS = Fatigue Severity Scale; ESS = Epworth Sleepiness Scale

Table 3. Sleep Behaviors and Sleep Parameters.

	CM		HC			
	Mean (SD)	**Range**	**Mean (SD)**	**Range**	**t**	**p**
Sleep Behavior						
Days with naps	7.43 (5.66)	0-23	3.10 (1.91)	0-8	-3.23	0.0025*
% of days with naps	25.85 (20.34)	0-85.19	11.22 (7.09)	0-28.57	3.04	0.0043
Nap duration (min)	88.72 (49.03)	8.75-208.7	80.20 (61.15)	11.67-228	-0.47	0.6441
Bed Time (hour:min)	23:25 (1:04)	21:08-1:09	23:47 (1:14)	22:01-2:45	1.02	0.3159
Rise Time (hour:min)	7:27 (1:08)	5:49-9:38	7:48 (1:00)	5:58-9:52	1.07	0.2897
TIB (min)	501.04 (56.34)	388.06-598.89	491.28 (42.14)	400.18-568.89	-0.62	0.5385
Diary-Based Sleep Data						
SOL (min)	29.11 (23.63)	6.00-112.04	10.15 (7.49)	0.91-33.00	-3.42	0.0024*
WASO (min)	28.12 (31.09)	3.39-132.78	12.70 (11.89)	1.25-44.58	-2.07	0.0489*
TWT (min)	57.23 (41.37)	10.48-181.5	22.85 (14.25)	6.96-52.22	-3.51	0.0012*
SE (%)	80.39 (10.01)	57.48-94.54	90.98 (5.76)	80.63-98.46	4.10	0.0003*
TST (min)	402.74 (47.58)	310.41-484.29	446.91 (45.39)	337.68-534.52	3.00	0.0047*
Actigraphy-Based Sleep Data						
SOL (min)	14.03 (11.02)	2.57-44.75	13.60 (12.48)	2.07-55.94	-0.12	0.9084
WASO (min)	37.39 (13.37)	19.48-73.52	39.57 (14.20)	12.36-71.46	0.50	0.6201
TWT (min)	65.45 (25.27)	36.90-136.6	70.35 (24.80)	31.86-134.8	0.62	0.5397
SE (%)	86.20 (5.06)	71.52-92.64	85.22 (4.75)	74.16-93.19	-0.63	0.5320
TST (min)	412.55 (40.55)	337.77-468.68	409.94 (34.45)	325.41-470.59	-0.22	0.8272

* p<.025 for days with naps; * p < .01 for Diary-Based SOL, WASO, TWT, SE, TST

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Note. CM = Chronic Migraine; HC = Healthy Control; SD = Standard Deviation; TIB = Time in
Bed; SOL = Sleep Onset Latency; WASO = Wake after Sleep Onset; TWT = Total Wake Time;
SE = Sleep Efficiency; TST = Total Sleep Time

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Table 4. Headache Severity Predicting Same Day Sleep Behavior

Independent Variable	Dependent Variable	b	SE	95% CI	t	p
Headache Severity	Nap (yes/no)	0.07	0.04	-0.01, 0.14	1.79	0.0735
Headache Severity	Nap duration (min)	6.08	2.05	2.01, 10.14	2.96	0.0037*
Headache Severity	Bed Time (~~hour:~~min from midnight)	-2.62	1.10	-4.78, -0.48	-2.39	0.0171
Headache Severity	Rise Time (~~hour:~~min) from midnight)	-0.30	1.21	-2.68, 2.08	-0.25	0.8057
Headache Severity	Time in Bed (min)	2.02	1.35	-0.63, 4.66	1.5	0.1344

* p<.0125 for Nap duration

Note. Headache severity was measured on a 0-10 scale indicating maximum headache severity. The nap variable was a dichotomous variable based on whether a nap was reported the same day as the headache severity rating. Nap duration was the mean duration of the nap on days when a nap was taken. Units for bed time and rise time are reported in minutes centered on midnight, such that negative values are before midnight and positive values are after midnight.

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Table 5. Sleep Behavior Predicting Same Night Sleep Efficiency

Independent Variable	Dependent Variable	b	SE	95% CI	t	p
Nap (yes/no)	Diary Sleep Efficiency (%)	-0.51	1.43	-3.31, 2.29	-0.36	0.7210
Nap duration (min)	Diary Sleep Efficiency (%)	-0.06	0.02	-0.10, -0.02	-3.27	0.0014*
Bed Time (~~hour:~~min from midnight)	Diary Sleep Efficiency (%)	~~-32.98~~0.02	~~11.36~~0.01	~~-55.29, -10.68~~-0.04, -0.01	-2.90	0.0038*
Rise Time (~~hour:~~min from midnight)	Diary Sleep Efficiency (%)	~~33.50~~0.02	~~10.35~~0.01	~~13.17, 53.82~~0.01, 0.04	3.24	0.0013*
Time in Bed (min)	Diary Sleep Efficiency (%)	0.02	0.01	0.01, 0.03	3.44	0.0006*
Nap (yes/no)	Actigraphy Sleep Efficiency (%)	-0.87	0.83	-2.49, 0.76	-1.05	0.2951
Nap duration (min)	Actigraphy Sleep Efficiency (%)	-0.04	0.01	-0.06, -0.02	-4.41	<.0001*
Bed Time (~~hour:~~min from midnight)	Actigraphy Sleep Efficiency (%)	~~-5.59~~0.004	~~6.73~~0.005	~~-18.82, 7.64~~0.01, 0.01	-0.83	0.4066
Rise Time (~~hour:~~min from midnight)	Actigraphy Sleep Efficiency (%)	~~32.68~~0.023	~~5.87~~0.004	~~21.15, 44.20~~0.01, 0.03	5.57	<.0001*
Time in Bed (min)	Actigraphy Sleep Efficiency (%)	0.02	0.00	0.01, 0.03	5.88	<.0001*

* p<.0125 for Nap duration
* p<.01 for Bed Time, Rise Time, and Time in Bed

Note. The nap variable was a dichotomous variable based on whether a nap was reported on that day. Nap duration was the mean duration of the nap on days when a nap was taken. Units for bed time and rise time are reported in minutes centered on midnight, such that negative values are before midnight and positive values are after midnight.

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Table 6. Sleep Behavior Predicting Same Night Total Sleep Time

Independent Variable	Dependent Variable	b	SE	95% CI	t	p
Nap (yes/no)	Diary TST (min)	-5.64	10.63	-26.52, 15.25	-0.53	0.5963
Nap duration (min)	Diary TST (min)	-0.21	0.14	-0.48, 0.06	-1.52	0.1319
Bed Time (~~hour:~~min from midnight)	Diary TST (min)	-0.57	0.05	-0.67, -0.46	-10.53	<.0001*
Rise Time (~~hour:~~min from midnight)	Diary TST (min)	0.67	0.05	0.58, 0.76	14.51	<.0001*
Time in Bed (min)	Diary TST (min)	0.91	0.03	0.85, 0.97	29.71	<.0001*
Nap (yes/no)	Actigraphy TST (min)	-8.57	9.21	-26.66, 9.52	-0.93	0.3523
Nap duration (min)	Actigraphy TST (min)	-0.25	0.13	-0.51, 0.01	-1.89	0.0613
Bed Time (~~hour:~~min from midnight)	Actigraphy TST (min)	-0.48	0.05	-0.58, -0.39	-10.31	<.0001*
~~Out of Bed (hour:~~Rise Time (min from midnight)	Actigraphy TST (min)	0.60	0.04	0.52, 0.67	15.19	<.0001*
Time in Bed (min)	Actigraphy TST (min)	0.79	0.03	0.74, 0.84	31.17	<.0001*

* p<.01 for Bed Time, Rise Time, and Time in Bed

Note. Headache severity was measured on a 0-10 scale indicating maximum headache severity. The nap variable was a dichotomous variable based on whether a nap was reported. Nap duration was the mean duration of the nap on days when a nap was taken. TST = Total Sleep Time. Units for bed time and rise time are reported in minutes centered on midnight, such that negative values are before midnight and positive values are after midnight.

Table 7. Sleep Predicting Next Day Headache Severity

Independent Variable	Dependent Variable	b	Std Err	95% CI	t	p
Diary TST (min)	Next Day Headache Severity	-0.13	0.07	-0.27, 0.00	-1.96	0.0505
Actigraphy TST (min)	Next Day Headache Severity	-0.11	0.08	-0.27, 0.05	-1.33	0.1843
Diary SE (%)	Next Day Headache Severity	-0.01	0.01	-0.03, 0.01	-0.99	0.3228
Actigraphy SE (%)	Next Day Headache Severity	-0.01	0.02	-0.04, 0.02	-0.92	0.3562

Note. TST = Total Sleep Time; SE = Sleep Efficiency; Std Err = Standard Error. Headache severity was measured on a 0-10 scale indicating maximum headache severity.