Naps and Circadian Rhythms in Postmenopausal Women

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Background. Napping patterns and relationships among naps, circadian rhythms, and nocturnal sleep were evaluated in postmenopausal women. Naps and nocturnal sleep were compared between depressed women and healthy volunteers.

Methods. The study included 436 postmenopausal women between the ages of 50 and 81 years. Psychiatric interviews were conducted using the Structured Clinical Interview for DSM-IV Axis I Disorders. Each participant wore a wrist-activity monitor and kept a daily sleep log at home for 1 week. The major urinary melatonin metabolite (6-sulfatoxymelatonin [aMT6s]) was measured for two 24-hour periods at home.

Results. There was no significant difference in naps and nocturnal sleep patterns between depressed participants (n = 30) and those with no history of mental disorder (n = 222). Three peaks occurred in the timing of napping: approximately 1 hour before bedtime, 8 to 9 hours after wake-up time, and 2 hours after waking, in descending order of magnitude. Significant inverse correlations were observed between evening nap duration and both wake-up time and aMT6s acrophase. The onset time of aMT6s excretion was advanced by 32 minutes in evening nappers.

Conclusions. Evening napping, a characteristic of these postmenopausal women, may be related to an advance of circadian rhythms in this age group. Relationships between evening napping and earlier wake-up time may be a common manifestation of advanced circadian rhythms or may be a homeostatic effect.

OUT-OF-BED naps have been investigated in relation to nocturnal sleep and circadian rhythms (1,2). Different patterns of napping between young and older persons have been reported, with the latter taking naps more often in the evening (3). Evening napping, either experimentally induced in the laboratory or observed in home environments, is related to nocturnal sleep and circadian rhythms. One study found that evening naps from 7:00 PM to 12:00 AM resulted in phase advances of melatonin and thyrotropin secretion (4). In another experimental study, an early evening nap lasting approximately 2 hours (from 6:00 PM) reduced rapid eye movement latency and decreased electroencephalographic power density in the delta and theta bands in the postnap night (5). We observed that healthy older adults who take evening naps woke earlier in the morning at home and had advanced melatonin and cortisol rhythms in the laboratory compared with older adults who do not take evening naps (6). The study of evening napping is relevant because it has been observed particularly in older adults (7,8) and might be explained in terms of changes of circadian rhythms in aging (9,10). Our previous findings on evening napping and its relation to nocturnal sleep and circadian rhythms (3,6) in older adults are extended here. Future studies should examine more representative samples that will further establish napping characteristics in aging.

In depressed patients, poor sleep efficiency, reduced slow-wave sleep, and reduced rapid eye movement latency have been consistently reported (11,12). These sleep disturbances could be experimentally induced by afternoon or evening naps (1,5). One epidemiologic study also showed that frequent daytime nappers reported more depressive symptoms than did infrequent nappers (13). Thus, we wanted to determine whether depressed persons have different patterns of napping compared with healthy persons.

We conducted the current study in a community-based volunteer sample of healthy postmenopausal women enrolled in the observational component at the San Diego Clinical Center for the Women’s Health Initiative. The specific aims were (a) to evaluate relationships among naps, circadian rhythms, and nocturnal sleep in postmenopausal women, and (b) to compare naps and nocturnal sleep in depressed persons and healthy volunteers.

METHODS

Participants

The Women’s Health Initiative Observational Study is a nonintervention component of the Women’s Health Initiative. Postmenopausal women aged 50 to 79 years were enrolled between 1994 and 1998 at 40 U.S. sites (14). An ancillary study to evaluate sleep and mood was conducted at the San Diego Clinical Center. The current ancillary study involved 436 volunteers who were 50 to 81 years old (67.8 ± 7.9 years; mean ± standard deviation). All participants were living independently in the community. No one was excluded because of medications or illnesses, except terminal cancer. Of the participants, 71.9% were white, 13.9% were Hispanic, 9.6% were African American, 3.9% were Asian, and 0.8% were Native American. Further data from this population have been described elsewhere (15,16). The study was approved by the Institutional Review Board of the University of California, San Diego. Each participant gave written informed consent.

Procedures

Data collection: Nocturnal sleep and naps.—Participants were asked to wear the Actillume wrist activity monitor.
(Ambulatory Monitoring, Inc., Ardsley, NY) and keep daily sleep logs at home for 1 week. Of the participants, 97.1% (423 of 436) provided 6 or 7 days of day-night data. We also obtained 5 days’ data from 6 participants, 4 days’ data from 4 participants, 3 days’ data from 2 participants, and 2 days’ data from 1 participant. The Actillume wrist activity monitor records wrist acceleration 20 times per second, with differences integrated every 10 seconds. The maximal activity score of each minute was the largest integrated activity over 10 seconds within each minute. Based on these maximal activity scores, automatic sleep scoring was calculated using Action3 software (Ambulatory Monitoring, Inc.) and previously validated algorithms (17,18). This automatic sleep scoring was edited with assistance of daily sleep logs, notes on illumination, and Webster’s rules (19). Naps were defined as “any short sleep episode” out of bed with no specification of duration (20).

Psychiatric interview.—Using the Structured Clinical Interview for DSM-IV Axis I Disorders, Non-patient Edition (SCID-NP) (21), psychiatric interviews were conducted by a board-certified psychiatrist (D.F.K.). Based on the SCID diagnoses, the participants were separated into 3 groups: (a) those having a mood disorder of any kind, depressive type, current; (b) those having a mood disorder of any kind, depressive type, past, or psychiatric diagnoses other than mood disorder; and (c) those having no current or past psychiatric Axis I diagnosis of any kind. The third group served as the control.

Urinary 6-sulphatoxymelatonin assays.—The participants were asked to collect every fractional urine sample during two 24-hour intervals, approximately 3 days apart. They were instructed to urinate approximately every 2 hours during the day and to collect all nocturnal voidings, which resulted in an average of 10 samples per 24 hours. Each urine sample was measured for volume, and a 2-ml aliquot was frozen at home and then later stored at −70°C. Urinary 6-sulphatoxymelatonin (aMT6s) was assayed using radioimmunoassay kits (ALPCO, Windham, NH). At a sample dilution of 1:125, the sensitivity of the assay was 0.2 ng/ml. Intraassay and interassay coefficients of variation were 3.3% and 6.7%, respectively.

Data Analysis

Nocturnal sleep and naps.—From wrist activity, the following nocturnal sleep parameters were inferred: bedtime, wake-up time, sleep latency, time in bed, total sleep time, waking time after sleep onset, and sleep efficiency. Bedtime and wake-up time were determined from illumination recordings, activity scores, and sleep logs. Out-of-bed naps were analyzed with reference to each day’s wake-up time and the following bedtime. These analyses covered 10 hours after wake-up time and 10 hours before bedtime, and they were calculated in 20-minute averages. The main advantage of this analytical approach is that clock-time averages may confound sleep in bed and out of bed, because the in-bed sleep periods vary from day to day and among participants. Evening naps were defined as out-of-bed sleep occurring from 2 hours to just before bedtime.

aMT6s analysis and phase relationship.—To ensure the reliability of the aMT6s data, profiles with atypical waveforms, suggesting faulty collection or assay interference, were blindly scored and excluded from the analysis, as previously described (15). We used 343 participants in the current aMT6s analysis. Twenty-four-hour cosine fits were applied to determine acrophases, amplitudes, and mesors (24-hour cosine mean). The times of aMT6s onset and offset were defined as the times of upward and downward crossing, respectively, of the mesor of aMT6s cosine fits. When of adequate quality, parameters from both collections for each participant were averaged.

With these data, the reliability of 2 onset estimates during the same week was $r = .72$ ($p < .001$). The reliability of offset estimates was $r = .44$ ($p < .001$). In another study using similar techniques, the mean of aMT6s onsets from 2 urine collections at home correlated $r = .59$ ($p = .002$), with onset estimated from samples collected several days later in the laboratory. The offsets correlated $r = .63$ ($p = .001$). To explore phase relationships between evening napping and circadian rhythms, the phase angle (time interval) measured from aMT6s onset to bedtime was calculated.

Statistical analysis.—We used SPSS 10.0 for Windows (SPSS, Inc., Chicago, IL) for the statistical analyses. We used Pearson correlation coefficients to determine the relationship among age, nap duration, and melatonin rhythms. We calculated partial correlations, controlled for age, diagnosis, and race, to evaluate the relationship between evening nap duration and melatonin rhythms. We compared parameters of nocturnal sleep, napping, and melatonin rhythms in evening and nonevening nappers using two-tailed $t$ tests. Significance was defined at $p < .05$.

RESULTS

Comparison Between Depressive Disorders and Control

Based on the SCID, 30 of 436 participants had current depressive disorders of any kind and 222 had no past or current psychiatric diagnoses. Depressed participants used antidepressants and sleeping aids more than controls did (chi-square test, $p < .01$, $p < .01$, respectively). There was no significant difference in nap duration and nocturnal sleep parameters between depressed participants and controls, although depressed participants took slightly longer naps than did controls (daytime, 41.5 minutes vs 32.8 minutes; evening, 8.8 minutes vs. 8.5 minutes). A similar contrast was observed between participants with major depressive disorder ($n = 13$) and controls.

Naps, Nocturnal Sleep, and aMT6s Rhythm

Naps and nocturnal sleep.—Figure 1 shows the timing of naps during the 10 hours after wake-up and 10 hours before bedtime ($n = 436$). Three peaks occurred in the nap analysis.
The highest peak occurred approximately 1 hour before bedtime, the second highest was approximately 8 or 9 hours after wake-up time, and the smallest was approximately 2 hours after wake-up time. The highest peak was approximately 1 hour before bedtime, the second highest was 8 or 9 hours after bedtime, and the smallest was approximately 2 hours after wake-up time.

Figure 1. The percentage of time that participants were asleep after waking in the mornings (top) and before bedtime (bottom). The Y axis represents the percentage of participants who are asleep at any given time interval, where each dot represents a 20-minute interval. Three peaks were observed. The highest peak was approximately 1 hour before bedtime, the second highest was 8 to 9 hours after wake-up time, and the smallest was approximately 2 hours after wake-up time.

The highest peak occurred approximately 1 hour before bedtime, the second highest was approximately 8 or 9 hours after wake-up time, and the smallest was approximately 2 hours after wake-up time. Bedtimes and wake-up times of the participants averaged (standard deviation) 23:02 ± 1:06 and 6:55 ± 1:01, respectively. The averaged all-day and evening nap durations were 31.3 minute/day and 7.75 minute/day, respectively. Table 1 shows correlations among participant age, naps, and wake-up times. Significant correlations occurred among age, all-day nap duration, and evening nap duration. All-day nap duration was significantly increased in participants between the ages of 70 and 81 years compared with participants who were 50 to 59 years or 60 to 69 years old (F statistic [2, 433] = 5.61; p < .01 by analysis of variance; p < .05 and p < .05 by post hoc Bonferroni test). Evening nap duration tended to increase with age and was higher in the 70- to 81-year-old group compared with the other 2 age categories (F statistic [2, 433] = 2.76; p = .064 by analysis of variance). A significant inverse correlation occurred between evening nap duration and wake-up time, but neither all-day nap nor nonevening nap duration correlated with wake-up time. There were no significant relationships between age and any sleep parameters, except that sleep efficiency was associated with age (r = .10, p < .05).

Naps and aMT6s rhythm.—Table 1 shows partial correlations between naps and aMT6s rhythm. In partial correlations, controlled for age, diagnosis, and race, there was a significant association between evening nap duration and aMT6s acrophase. Evening nap duration was not significantly associated with the clock time of aMT6s onset, but the phase angle of aMT6s onset to sleep onset was significantly related to evening nap duration in a similar partial correlation analysis. That is, the longer before bedtime aMT6s excretion increased, the more evening napping occurred. There were significant correlations between aMT6s onset and bedtime (r = .254, p < .01), between aMT6s offset and wake-up time (r = .348, p < .01), between aMT6s acrophase and bedtime (r = .239, p < .01), and between aMT6s acrophase and wake-up time (r = .419, p < .01).

### Table 1. Correlations (r) and Partial Correlations (r_p) Between Age, Naps, Nocturnal Sleep, and Circadian Rhythms of aMT6s

<table>
<thead>
<tr>
<th>Parameters</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age—all-day nap duration (r)</td>
<td>.169</td>
</tr>
<tr>
<td>Age—evening nap duration (r)</td>
<td>.123</td>
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<tr>
<td>Evening nap duration—wake-up time (r)</td>
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</tr>
<tr>
<td>All-day nap duration—wake-up time (r)</td>
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</tr>
<tr>
<td>Nonevening nap duration—wake-up time (r)</td>
<td>-.026</td>
</tr>
<tr>
<td>Evening nap duration—aMT6s acrophase (r_p)</td>
<td>-.115</td>
</tr>
<tr>
<td>Evening nap duration—aMT6s onset (r_p)</td>
<td>-.102</td>
</tr>
<tr>
<td>Evening nap duration—phase angle (r_p)*</td>
<td>.135</td>
</tr>
</tbody>
</table>

*Phase angle of aMT6s onset and sleep onset in hours.

### Notes
- aMT6s = 6-sulphatoxymelatonin.
- *p < .01; †p < .05.

Evening Versus Nonevening Nappers

Evening nappers were defined as participants who averaged evening naps of more than 5 minutes per day. Evening nap duration was calculated from a mean across all days of recording. Table 2 shows a comparison of naps, nocturnal sleep, and aMT6s rhythms in evening and nonevening nappers. There were no age differences between evening and nonevening nappers (p = .084). Decreased wake time after sleep onset and increased sleep efficiency, more daytime napping, and more napping at other times than evening were observed in evening nappers compared with nonevening nappers (all, p < .01). In evening nappers, aMT6s onset was advanced by 32 minutes (p < .05), and the phase angle of aMT6s onset to sleep onset was increased in evening nappers (p < .05). Wake-up time was advanced by 10 minutes in evening nappers, although not significantly (p = .092).
Table 2. Naps, Nocturnal Sleep, and Circadian Rhythms of aMT6s Between Evening Nappers and Nonevening Nappers

<table>
<thead>
<tr>
<th></th>
<th>Evening Nappers</th>
<th>Nonevening Nappers</th>
<th>p Value</th>
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<td><strong>Naps and sleep</strong></td>
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<tr>
<td>N</td>
<td>N = 176</td>
<td>N = 260</td>
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<tr>
<td>Bedtime</td>
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<td>23:03 ± 1:00</td>
<td>.961</td>
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<tr>
<td>Wake-up time</td>
<td>06:49 ± 0:58</td>
<td>06:59 ± 1:02</td>
<td>.092</td>
</tr>
<tr>
<td>All-day napping (min)</td>
<td>49.0 ± 36.8</td>
<td>19.3 ± 22.6</td>
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<tr>
<td>Nonevening napping (min)</td>
<td>31.8 ± 30.8</td>
<td>18.1 ± 22.3</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>TST (min)</td>
<td>364.6 ± 56.9</td>
<td>357.0 ± 52.4</td>
<td>.149</td>
</tr>
<tr>
<td>SE (%)</td>
<td>83.3 ± 7.0</td>
<td>80.8 ± 7.3</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>WASO (min)</td>
<td>79.1 ± 32.1</td>
<td>92.8 ± 36.7</td>
<td>&lt;.01</td>
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<td>aMT6s Parameters</td>
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<td></td>
</tr>
<tr>
<td>N</td>
<td>N = 141</td>
<td>N = 202</td>
<td></td>
</tr>
<tr>
<td>aMT6s Onset</td>
<td>22:29 ± 1:56</td>
<td>23:01 ± 2:04</td>
<td>&lt;.05</td>
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<tr>
<td>aMT6s Acrophase</td>
<td>3:55 ± 2:53</td>
<td>4:12 ± 2:44</td>
<td>.383</td>
</tr>
<tr>
<td>aMT6s Offset</td>
<td>8:24 ± 2:11</td>
<td>8:46 ± 1:45</td>
<td>.080</td>
</tr>
<tr>
<td>*Phase angle</td>
<td>0.57 ± 2.05</td>
<td>0.03 ± 2.03</td>
<td>&lt;.05</td>
</tr>
</tbody>
</table>

Notes: *Phase angle of aMT6s onset to sleep onset in hours. Values are mean ± SD (standard deviation).

aMT6s = 6-sulphatoxymelatonin; TST = total sleep time; SE = sleep efficiency; WASO = wake-up time after sleep onset.

**DISCUSSION**

In the current study, actigraphy monitoring revealed that late evening was the most characteristic time of napping. This result is consistent with previous reports on evening napping in aging samples (3,7,8). The second highest peak was observed in the afternoon, as has been described in the biphasic pattern of sleepiness seen in younger persons (22,23). Early morning napping, the third peak in this study, was previously observed by polysomnographic recording in a similar sample (8) and in an earlier actigraphic study (7). The above 3 peaks in the timing of out-of-bed napping suggest that the biphasic pattern of sleepiness of younger adults may gradually change to a polyphasic sleep pattern in older adults (13,24).

Consistent with the findings of other studies (25,26), increasing age was related to increasing duration of napping both in the evening and at other times than evening. Nocturnal sleep was not more disturbed in the oldest participants in the current study. Considering that increasing age was associated with increased prevalence of hypersomnia in older community samples (27), the current results of increases in daytime napping and no prominent changes in nocturnal sleep in aging are plausible. Like increases in the prevalence of hypersomnia (27), daytime napping was significantly increased in participants who were 70 years and older compared with those younger than 70 years, suggesting that an age-related threshold effect may contribute to the increase in daytime napping. Interestingly, an increased mortality risk has been reported for persons who sleep 8 hours or more at night (28) and for persons who frequently nap during the day (13,29). The risks associated with long sleep (daytime and nocturnal) need to be studied and confirmed in postmenopausal participants.

Napping in the evening, when maximal alertness is expected (30), may be a sign that the alerting signal from the suprachiasmatic nucleus might be weakened in these postmenopausal women. Conversely, several findings in this study support the proposition that evening napping is related to a relative advance of circadian rhythms as referenced to sleep. We noted significant associations among evening nap duration, aMT6s acrophase, and the phase angle of aMT6s onset to sleep onset. In evening nappers, compared with nonevening nappers, aMT6s was advanced and the phase angle of aMT6s onset and sleep onset was increased. Evening napping was also significantly, although weakly, associated with earlier wake-up time. The relationship between evening napping and earlier wake-up time might be a common manifestation of advanced circadian rhythms. Another explanation for the relationship between evening napping and earlier wake-up time is that the decrease in the homeostatic drive for sleep (31,32) after an evening nap could cause earlier wake-up time. However, the explanation based on homeostatic principle is less plausible in these postmenopausal women, because evening nappers showed increases in sleep efficiency and decreases in waking during nocturnal sleep compared with nonevening nappers. Increased napping at times other than evening and less nocturnal waking in evening nappers suggest that they might have greater sleep needs or trait sleepiness (33).

In the current study, we observed no differences in naps or any of other sleep parameters between depressed participants and controls. Depressed women tended to have lower sleep efficiency, more frequent nocturnal waking, and increased daytime napping, but differences were not significant. Considering some evidence that differences in sleep patterns between depressed persons and controls became greater with aging (34), this result was rather unexpected. However, the small sample size of depressed persons (n = 33) compared with controls (n = 220) limited the statistical power of these analyses. Drugs such as antidepressants and sleeping aids also could influence the results, and their depressive symptoms might be insufficient to cause significant sleep disturbances (as evidenced by the fact that the participants were living independently in the community).

A limitation of our study is the modest inaccuracy of the actigraphic method for assessing out-of-bed napping. Periods of wakefulness without gross movements could be mistakenly scored as sleep. More studies with 24-hour home polysomnography are needed to substantiate napping observed in this study. Nonetheless, because the amount of napping recorded by the Actillume wrist activity monitors shows 85% to 91% agreement and 0.9 to 0.98 correlations with polysomnography (17), it is unlikely that these results are artifactual.

Another limitation of the study is that the circadian rhythms of aMT6s might have been masked by room illumination (35). In addition, based on findings that older men take more naps than did older women (13,29) and that there are some sex differences in aging in nocturnal sleep (36,37), caution is warranted in applying the results of the current study to all older persons.

**Conclusion**

Evening napping, distinctively observed in the postmenopausal women in this study, may be explained in part by an advance of circadian rhythms in this age group. Relationships between evening napping and earlier wake-up...
time, although weak, may represent a common manifestation of advanced circadian rhythms or a homeostatic effect. Characteristics of naps and of nocturnal sleep in depressed persons should be further explored with larger depressed samples and with the exclusion of possible good drug effects.

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