Meal timing and subjective sleep disturbances in older men

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ARTICLE INFO
Section Editor: Michal Masternak
Keywords: Chrononutrition Insomnia Elderly Sleep disturbances Aging

ABSTRACT
Older adults often complain about sleep disturbances, such as difficulty falling asleep and difficulty maintaining sleep in the early morning hours. Here, we investigated whether meal timing is associated with sleep problems in a cohort of older Swedish men (n = 998, mean age 71). Each participant filled out a seven-day food diary used to determine the daily eating time window, daily eating midpoint, and meal timing variability (i.e., the variance in daily eating midpoints over seven days). Questionnaires were used to assess difficulty initiating sleep and difficulty maintaining sleep. As indicated by logistic regression adjusted for potential confounders (e.g., BMI, diabetes status), no significant associations were found between the meal timing parameters and subjective sleep problems (P ≥ 0.37). Similar results were obtained when restricting the analysis to adequate reporters of daily energy intake. Therefore, our findings suggest that meal timing variations do not contribute to subjective sleep problems in older men. Our results must be replicated in cohorts that also include women and other measures of pharmacological sleep aids is that users may suffer from rebound insomnia once the treatment is ceased (Chouinard, 2004). With these side effects in mind, it would be useful to find non-pharmacological interventions to aid sleep among older adults.

1. Introduction

Sleep in older adults differs from that of younger adults in many regards. Older adults more often complain about difficulty falling asleep, frequent awakenings after sleep onset, lighter sleep, advanced sleep timing (i.e., earlier bedtimes and rise times), and difficulty maintaining sleep in the early morning hours (Bliwise, 2016; Ohayon et al., 2004). There are several explanations for these age-related sleep changes, including impaired functioning of brain regions involved in the regulation of sleep and circadian rhythms (Mander et al., 2017; Wang et al., 2015), as well as the presence of sleep-disruptive conditions such as hypertension and frequent nighttime urination breaks (Vitiello, 2009). Thus, it is not surprising that the use of prescription sleep aids exhibits a significant increasing linear trend by age. Compared to the youngest age group (those aged 20–39), the reported use of prescription sleep aids increases from 1.8% to 5.7% among those aged 70–79 (Chong et al., 2013). While hypnotic drugs are effective in mitigating sleep problems such as difficulty falling asleep, they can cause side effects, e.g., next-day drowsiness and cognitive impairment (Huedo-Medina et al., 2012). An additional problem of

Abbreviations: BMI, body mass index; DIS, difficulty initiating sleep; DMS, difficulty maintaining sleep; HDI, healthy diet indicator; ICD, international classification of diseases; LUTS, lower urinary tract symptoms; OGTT, oral glucose tolerance test; PA, physical activity; TRE, time-restricted eating; ULSAM, Uppsala Longitudinal Study of Adult Men

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https://doi.org/10.1016/j.exger.2020.111089
Received 11 June 2020; Received in revised form 1 September 2020; Accepted 3 September 2020
Available online 07 September 2020
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may also influence sleep. For example, in fruit flies, food access limited to 12 hours every day increases daytime activity scores, reduces daytime sleepiness, and increases nighttime sleep (Gill et al., 2015). Similar effects of time-restricted eating (TRE) on sleep have been reported for humans. Long-term TRE improved sleep quality at night and elevated alertness during the day in overweight subjects or patients with metabolic syndrome (De Cabo and Mattson, 2019; Wilkinson et al., 2020).

Whether TRE may associate with sleep in older adults is, however, not clear. It could, for instance, be hypothesized that an earlier daily eating offset may reduce the risk of gastroesophageal reflux symptoms in the night, which can lead to impaired sleep (Lim et al., 2018). Meal timing can alter clock gene oscillations and photic responses in the suprachiasmatic nuclei of mice exposed to a light/dark cycle (Mendoza et al., 2005). Thus, it could also be speculated that humans who exhibit large variation in the daily eating midpoint may have less robust circadian rhythms, with possible adverse effects on sleep.

To investigate the association of the daily eating time window and eating midpoint variability with sleep in older adults, in the present study, we used cross-sectional data from the age-70 investigation of the Swedish Uppsala Longitudinal Study of Adult Men (ULSAM). We hypothesized that a shorter daily eating time window would reduce the risk of having difficulty initiating sleep (DIS) and difficulty maintaining sleep (DMS). We also expected that those with greater eating midpoint variability would experience DIS and DMS more often.

2. Material and methods

2.1. Population and study design

In 1970, 2322 men aged 50 years participated in ULSAM (please see http://www.pubcare.uu.se/ULSAM), which primary aim was to investigate the association of health parameters with disease and lifestyle factors from middle-age to later life. In 1990, 1211 men were re-examined (age 70-investigation). During this follow-up investigation, subjects filled out a seven-day food diary and responded to questions about sleep. For the present study, which represents a secondary analysis, sleep records, dietary records, and covariate information were only available for 998 participants (82.4% of the subjects that were re-examined at age 70). The 998 men in the final sample did not differ in age from the full cohort (final sample vs. full cohort, 71.0 ± 0.67 vs. 1.0 ± 0.6 years, P = 0.117, independent t-test). The study was performed in accordance with the declaration of Helsinki and received approval from the Ethical Regional Review Board Uppsala (Dnr 251/90, approved 1990–12–05).

2.2. Sleep

Participants’ sleep was examined by the following questions: “Do you have difficulties falling asleep at night?” (from here on referred to as “difficulty initiating sleep”, DIS) and “Do you often wake up in early hours, unable to get back to sleep?” (from here on referred to as “difficulty maintaining sleep”, DMS). Participants could either answer with “yes”, “no”, or “I don’t know” (n = 2 answering “I don’t know” for DIS, n = 10 for DMS, respectively; counted as no). Neither of these questions specifies a time referent.

2.3. Dietary assessment

All participants documented the content and timing of their meals in a pre-coded menu-book for seven consecutive days. Adequate dietary reporting was evaluated using the Goldberg 2 cut-off for adequate energy intake reports as modified by Black (2000).

The daily eating time window was computed based on the time interval between the first (eating onset) and last (eating offset) meal for each participant. The daily eating midpoint was defined as the midpoint between the first and last meal of the day (e.g., 08:00 h and 18:00 h, eating midpoint: 13:00 h). The daily eating time window and daily eating midpoint were averaged across the seven days for the analysis. Meal timing variability was estimated using the standard deviation of each participant’s daily eating midpoint over the seven days.

2.4. Potential confounders

All covariates were measured at age 70. For a detailed methodological description of the covariates, please find http://www.pubcare.uu.se/ulsam.

Diabetes prevalence was diagnosed via an Oral Glucose Tolerance Test (OGTT). Here, participants ingested 75 g glucose dissolved in 300 mL of water. Plasma glucose and insulin were measured before and 30, 60, 90, and 120 min after ingestion. Diabetes was diagnosed when the 120 min and one or more of the 30–90 min glucose values were ≥11.1 mmol/l (binary variable). Diseases of the circulatory system (ICD 390-459, I00-I99) were measured using the Swedish Hospital Discharge Register. Subjects diagnosed with a disease of the circulatory system before or during the age-70 investigation were coded as 1, otherwise as 0. The following two questions were used to examine lower urinary tract symptoms (LUTS): “Do you have difficulty in passing water?” and “Has the flow of urine become thin and weak?” Answering “I don’t know” (n = 16 and n = 56, respectively) was treated as no. Responding ‘yes’ to a minimum of one of these questions was defined as having LUTS. Frequent use of sleep medication was also included as a possible confounder. Participants answered the question, “Do you take sleeping pills more than three times a week?” with answer options being “yes”, “no”, or “I don’t know” (n = 5, counted as no).

BMI (kg/m²; continuous variable) was measured during a physical examination. Leisure-time physical activity (PA) was entered as a binary variable into the analysis (non-regular vs. regular PA), with regular PA representing the participant performing an active sport or heavy gardening ≥3 h/week and/or hard physical training or engaging in a competitive sport. Exact age, current smoking status (binary variable), and educational background (university education vs. upper secondary school (sixth form) or below; converted to a binary variable) were assessed via questionnaires or interviews.

As diet quality can affect our analysis, the Healthy Diet Indicator score (HDI) was calculated using all food items from the food diary (Van Egmond et al., 2019). The HDI is based on the dietary guidelines from the World Health Organization. The food components included are saturated fatty acids, polyunsaturated fatty acids, proteins, total carbohydrates, sucrose, fiber, fruit and vegetables, cholesterol, and fish. Modifications in the nutrient cut-off values were made to match the Swedish national guidelines better. The HDI score ranged from −1 to 8 points, with eight being highly adherent to the diet.

2.5. Statistical analysis

All analyses were performed using IBM SPSS Statistics 24 (SPSS Inc. Chicago, IL, USA).

Logistic regression was used to investigate the association of the daily eating time window and eating midpoint variability with sleep (i.e., DIS and DMS) in the full cohort, as well as in the subgroup of adequate reporters of energy intake. Results from unadjusted and adjusted logistic regressions are shown. In the adjusted analysis, all predictors of interest were entered into the model (i.e., daily eating time window, daily eating midpoint, and eating midpoint variability), as well as covariates of no interest (HDI, exact age, BMI, diabetes status, disease of the circulatory system status, smoking, physical activity, educational status, use of sleep medication, and lower urinary tract symptoms). Overall, a p-value < 0.05 was considered significant.
Table 1

| Variables                        | Total cohort |
|----------------------------------|--------------|
| Number of subjects               | 998          |
| Exact age (years)                | 71.0 ± 0.6 (69.0, 74.0) |
| BMI (kg/m²)                      | 26.2 ± 3.3 (17.0, 46.0) |
| Difficulty initiating sleep (%)  | 10.8         |
| Difficulty maintaining sleep (%) | 18.4         |
| Use of sleep medication (%)      | 4.4          |
| Diseases of the circulatory system (%) | 29.6       |
| Diabetes diagnosis (%)           | 13.7         |
| Lower urinary tract symptoms (%) | 29.1         |
| Currently smoking (%)            | 19.6         |
| Regular physical activity (%)    | 62.2         |
| University education (%)         | 17.1         |
| HDI score                        | 3.5 ± 1.8 (−1.0, 8.0) |
| Eating onset (hh:mm)             | 06:23 ± 01:16 (05:00, 10:00) |
| Eating offset (hh:mm)            | 18:04 ± 00:42 (12:42, 23:06) |
| Eating duration (hh:mm)          | 11:41 ± 01:26 (06:06, 18:06) |
| Eating midpoint (hh:mm)          | 12:14 ± 00:44 (09:36, 15:06) |
| Eating midpoint variability (hh:mm) | 00:34 ± 00:30 (00:00, 03:28) |

Values are expressed as mean ± SD (min, max), unless otherwise specified. *ICD 390-459, 100-199. Abbreviations: BMI, body mass index; HDI, Healthy Diet Indicator.

3. Results

3.1. Cohort characteristics

The cohort characteristics can be found in Table 1. Overall, 10.8% and 18.4% of the men experienced difficulties initiating sleep (DIS) and difficulties maintaining sleep (DMS), respectively. 4.4% of the men took sleep medication. A strong connection was found between the use of sleep medication and the sleep exposure variables. Specifically, we found that men reporting insomnia symptoms had a higher prevalence of using sleep medication (at least 3 times per week) compared to those without subjective sleep disturbances (sleep medication use among men without sleep disturbances vs. those reporting one of the insomnia symptoms vs. those reporting both insomnia symptoms: 0.8% vs. 12.0% vs. 28.2%, P < 0.001, Chi square test).

The participants were slightly overweight (BMI = 26.2), and 62.2% were regularly physically active. Participants started eating at 06:23 h and stopped at 18:04 h. As shown in the “feedogram” in Fig. 1, large inter-individual variations in the eating onset were detected. On average, the daily eating duration spanned 11:41 h, with an eating midpoint at 12:14 h.

3.2. Meal timing and sleep

Firstly, we performed unadjusted analyses using binary logistic regression, in order to investigate any bivariate associations between either of our variables of interest (i.e., eating duration, eating midpoint, and meal timing variability) and DIS or DMS in our full cohort. Here, no significant associations were found (p ≥ 0.12). Secondly, a fully adjusted binary logistic regression model was run for each of the sleep problems, including the variables of interest and covariates, yielding similar null-results (p ≥ 0.37).

As inadequate reporting of energy intake might have biased our results, we examined associations between meal timing parameters and sleep disturbances among men with adequate reports of energy intake in a subgroup-analysis (n = 529). As shown in Table 2, no significant associations were found in either the unadjusted (p ≥ 0.216) or the fully adjusted model (p ≥ 0.39), see Table 2.

4. Discussion

Time-restricted eating (TRE) has myriad positive effects on health, such as improved insulin sensitivity and weight loss (De Cabo and Mattson, 2019; Gill and Panda, 2015; Wilkinson et al., 2020). As TRE has also been shown to result in improved subjective sleep satisfaction and higher daytime alertness in metabolically unhealthy humans (Gill and Panda, 2015; Wilkinson et al., 2020), we investigated whether it would also link with better sleep in a cohort of older men. Older humans often experience sleep problems, such as difficulty falling asleep and long periods of wake after sleep onset (Blissire, 2016; Ohayon et al., 2004). Utilizing seven-day food registrations and sleep questions from 998 older men at age 71, we found that the daily eating time window exhibited considerable variance in this elderly cohort, which was primarily driven by inter-individual differences in eating onset. We also found that 10.8% and 18.4% of the cohort had difficulty initiating sleep (DIS) and difficulty maintaining sleep (DMS), respectively. However, we did not find robust evidence for the hypothesis that shorter daily eating time windows associate with a lower risk of suffering from either DIS or DMS while controlling for the daily eating midpoint. One explanation for the discrepancy between our findings and those obtained in metabolically unhealthy humans (Gill and Panda, 2015; Wilkinson et al., 2020) could be that our study was cross-sectional. Thus, better sleep may occur over time in response to TRE, as suggested by others (Gill and Panda, 2015; Wilkinson et al., 2020). It could also be that the sleep-improving effects of TRE decrease with age. Supporting this assumption, a four-week TRE intervention in a small sample of older individuals (65+ years old) did not alter reports of physical or mental fatigue (Anton et al., 2019). A third explanation for these discrepant findings could be that we used two questions to assess sleep in older subjects, whereas studies in metabolically unhealthy participants utilized multiple measures of sleep (e.g., 14 weeks of daily ratings of sleep satisfaction, repeated measurements of 24-hr actigraphy, and a 19-item sleep questionnaire; see Wilkinson et al., 2020).

The 24-hr sleep-wake cycle is intimately linked with our internal clock (Borbély et al., 2016). Hence, any measure that will improve the alignment of our endogenous circadian rhythm with the external light/dark cycle is likely to aid sleep. The most important external zeitgeber (timing cue) is the light/dark cycle. In addition to light, 24-hr meal timing and physical activity patterns also act as non-photic cues to align the endogenous circadian rhythms with the external 24-hr day in humans (Wehrens et al., 2017; Youngstedt et al., 2019). Aging is associated with decreased circadian rhythmicity of behaviors, including
sleep (Mattis and Sehgal, 2016). Thus, adhering to a consistent meal timing pattern may help stabilize circadian rhythmicity in older men and have positive effects on sleep. With this in mind, we also examined whether the variation of the daily eating midpoint over one week as a measure of meal timing variability would associate with subjective sleep problems among older men. However, the results from this analysis did not support our hypothesis, as no significant associations were found. Aging decreases the effect of monochromatic blue light (456 nm) on clock gene expression, subjective alertness, sleepiness, and mood in older, as compared to young individuals (Daneault et al., 2016). This suggests that aging reduces the sensitivity of the internal clock to light. Based on our findings, it could also be speculated that aging may also reduce the potential of consistent meal timing patterns to entrain the internal clock in humans.

A small study in healthy young adults has recently shown that shifting the eating midpoint by 5 h did not affect plasma melatonin and cortisol rhythms, both well-validated markers of the activity of the central pacemaker (i.e., suprachiasmatic nuclei). Additionally, no effects of shifted meal timing on subjective sleepiness and objective markers of sleep assessed by actigraphy were found (Wehrens et al., 2017). In line with these findings, no association between the daily eating midpoint and subjective sleep disturbances was found in the present study.

Several strengths and limitations apply to our study. A strength of our study is that the cohort consisted of men of similar age. Additionally, all men were from the same region (i.e., Uppsala county). We also controlled our analysis for various important confounders that affect sleep, such as lower urinary tract symptoms and sleep medications. Finally, findings in the full cohort were confirmed in a sub-cohort of men with adequate daily energy intake reports. This reduced the risk that under-reporting may have biased our results.

Several limitations apply to our study. In the present study, reports of DIS and DMS were used as binary outcome variables. The number of insomnia symptoms was strongly connected with sleep medication use in the present study, suggesting that these variables may represent meaningful proxies of sleep problems. However, the questions used to assess these sleep problems were not designed to provide insight into duration, frequency, and severity of subjective insomnia symptoms, limiting the generalizability of our findings and, therefore, warrants further investigation. Another limitation of our study is that meal characteristics may associate with sleep variables not measured herein, such as sleep duration. We did not have information about napping either, which increases in later life: 10% of adults ages 55–64, and 25% ages 75–84, report daytime naps (Foley et al., 2007). Finally, it is not clear whether our results can be extrapolated to older females, which more often have insomnia (Brabbin et al., 1993) and exhibit differences in their dietary habits compared to men (Hunter and Linn, 1979).

Notwithstanding these limitations, our findings do not suggest that TREL and a high degree of meal timing stability may offset subjective sleep problems in older men.

CRediT authorship contribution statement

Conceptualization, Lieve T. van Egmond and Christian Benedict; Data curation, Lieve T. van Egmond, Thiago C. Moulin and Tommy Cederholm; Formal analysis, Lieve T. van Egmond, Thiago C. Moulin, Tommy Cederholm and Christian Benedict; Funding acquisition, Helgi B. Schiöth and Christian Benedict; Investigation, Lieve T. van Egmond and Tommy Cederholm; Methodology, Lieve T. van Egmond, Thiago C. Moulin and Christian Benedict; Project administration, Lieve T. van Egmond; Supervision, Helgi B. Schiöth and Christian Benedict; Writing – original draft, Lieve T. van Egmond, Thiago C. Moulin and Christian Benedict; Writing – review & editing, Helgi B. Schiöth and Tommy Cederholm. All authors have read and agreed to the published version of the manuscript.

Funding

This research was funded by Novo Nordisk Foundation (C.B., grant number NNF14OC0009349), Swedish Brain Foundation (C.B., grant number FO2019-0028), Swedish Research Council (C.B., grant number 2015-03100), and Royal Swedish Academy of Sciences (T.C.M.).

Declaration of competing interest

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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Table 2

| Difficulty initiating sleep | Full cohort | Adequate responders |
|----------------------------|------------|-------------------|
| Unadjusted | Adjusted | Unadjusted | Adjusted |
| OR [95%-CI] | P | OR [95%-CI] | P | OR [95%-CI] | P | OR [95%-CI] | P |
| Eating duration | 0.93 [0.81–1.07] | 0.30 | 0.96 [0.81–1.16] | 0.73 | 0.99 [0.89–1.11] | 0.86 | 1.00 [0.87–1.15] | 0.96 |
| Eating midpoint | 1.24 [0.95–1.63] | 0.12 | 1.11 [0.77–1.61] | 0.58 | 1.00 [0.80–1.25] | 1.00 | 0.99 [0.74–1.33] | 0.96 |
| Meal timing variability | 1.25 [0.86–1.82] | 0.24 | 1.23 [0.79–1.91] | 0.37 | 0.94 [0.68–1.30] | 0.71 | 0.88 [0.61–1.26] | 0.47 |
| Difficulty maintaining sleep | Unadjusted | Adjusted |
| OR [95%-CI] | P | OR [95%-CI] | P |
| Eating duration | 1.04 [0.71–1.54] | 0.83 | 1.11 [0.60–2.04] | 0.74 | 0.93 [0.66–1.30] | 0.66 | 1.06 [0.63–1.79] | 0.83 |
| Eating midpoint | 1.01 [0.82–1.23] | 0.95 | 1.03 [0.78–1.34] | 0.86 | 1.07 [0.90–1.27] | 0.44 | 1.11 [0.88–1.41] | 0.39 |
| Meal timing variability | 0.77 [0.43–1.40] | 0.39 | 0.87 [0.41–1.85] | 0.71 | 1.03 [0.65–1.64] | 0.91 | 1.11 [0.64–1.92] | 0.71 |

Data are shown as OR [95%-CI]. Abbreviations. CI: confidence interval; OR: Odds ratio; P: p-value.
