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Sleep duration and quality in relation to semen quality in healthy men screened as potential sperm donors

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ABSTRACT

Background: Short sleep duration and poor sleep quality are increasingly prevalent in modern society and may be associated with impaired semen quality, yet studies are inconclusive.
Objectives: To investigate the reproducibility of semen quality parameters among 842 healthy men screened as potential sperm donors and explore the associations of sleep duration and quality with repeated measures of semen quality parameters.
Methods: We assessed sleep duration (night sleep and daytime napping) and sleep quality using the Pittsburgh Sleep Quality Index (PSQI) among 842 healthy men screen as potential sperm donors. We examined sleep characteristics in relation to repeated measurements (n = 5601) of semen parameters using linear mixed-effects models.
Results: High degrees of within-individual variability were found for total and progressive sperm motility with intraclass correlation coefficient (ICC) of 0.20 and 0.22, respectively; while fair-to-good reproducibilities were observed for sperm volume, concentration, and total count (ICC = 0.54, 0.62, and 0.50, respectively). Compared to men with total sleep duration of 8.0–8.5 h/day (h/d), men who slept less than 6.0 h/d and higher than 9.0 h/d had lower sperm volume of 12% [95% confidence interval (CI): −22%, −0.68%] and 3.9% (95% CI: −7.3%, −0.44%), respectively. Compared to men with night sleep duration of 7.5–8.0 h/d, men who slept less than 6.0 h/d had lower total and progressive sperm motility of 4.4% (95 CI:−8.4%, −0.24%) and 5.0% (95% CI: −9.2%, −0.48%), respectively. Compared to men who reported good sleep quality (total PSQI score ≤5.0), those reporting poor sleep quality (total PSQI score > 5.0) had lower total sperm count, total motility, and progressive motility of 8.0% (95% CI: −15%, −0.046%), 3.9% (95% CI: −6.2%, −1.5%), and 4.0% (95% CI: −6.5%, −1.4%), respectively.
Conclusions: Both long and short sleep duration and poor sleep quality were associated with impaired semen quality parameters. The high within-individual variability of total and progressive sperm motility suggests that a single measurement may result in a moderate degree of classification error.

1. Introduction

A decline in semen quality has been widely reported across several countries, (Carlsen et al., 1992; Huang et al., 2017; Levine et al., 2017; Mishra et al., 2018; Swan et al., 1997), however, little is known about the causes or impact of such changes. Lifestyle factors, including the

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increased prevalence of short sleep duration and poor sleep quality (Bin, 2016; Knutson et al., 2010), are potential risk factors. Sleep is a naturally recurring behavior that is modulated by circadian rhythms. Inadequate sleep duration has been linked to adverse health outcomes, including all-cause mortality (Wang et al., 2018), cardiovascular diseases (Dominguez et al., 2019), hypertension (Kim et al., 2018), and diabetes (Shan et al., 2015).

Several studies have investigated the association of sleep duration with male semen quality or fecundability, however, results are inconsistent. For instance, Shi et al. (2018) revealed a monotonously positive association between sleep duration and sperm concentration among 328 men who underwent semen examination. In contrast, Wise and colleagues reported that short and long sleep duration were associated with reduced couple fecundability, an important consequence of poor semen quality (Wise et al., 2018). Liu et al. (2017) revealed that both short and long sleep duration were associated with reduced sperm count, survival rate, or motility among 981 healthy men. Chen et al. (2016) also revealed an inverse U-shaped association between sleep duration and sperm volume and total count among 796 college students. Most previous studies ignored potential within-individual variability in semen quality parameters and collected semen samples at a single time point, which may potentially lead to classification error and further bias risk estimation (Chiu et al., 2017; Francavilla et al., 2007; Keel, 2006; Leushuis et al., 2010; Poland et al., 1986). Moreover, growing evidence indicates that sleep quality is also a valuable measure of sleep (Bin, 2016). To date, however, few studies have simultaneously assessed the associations of sleep duration and quality with semen quality parameters.

In this study, we assessed the reproducibility of semen quality parameters among healthy men screened as potential sperm donors and explored the associations of sleep duration and quality with repeated measures of semen quality parameters.

2. Materials and methods

2.1. Study design

From April 2017 to July 2018, we recruited 1487 male participants who volunteered as potential sperm donors at the Hubei Province Human Sperm Bank, and details of the study design have been described previously (Chen et al., 2019; Sun et al., 2019). Participants were first checked for eligibility of potential sperm donors if they met the following criteria: (1) aged between 22 and 45 years; (2) had no less than a high school degree; and (3) had no genetic or sexually transmitted diseases (e.g., syphilis, gonorrhea, HIV, and hepatitis, etc.). All potential donors then completed an initial semen screening examination to check for the semen quality, and men who met the donation criteria from the Chinese Ministry of Health (2003) (i.e., fresh semen samples should have a sperm concentration $\geq 60 \times 10^6$/mL, progressive motility ≥60%, and percentage of normal morphology > 30%; post-thaw semen samples should have a progressive motility ≥40%, number of motile sperm per vial $\geq 12 \times 10^6$, and frozen-thaw survival rate ≥60%) were requested to provide a sufficient number of semen specimens to impregnate up to 5 women within 6 months. Semen quality was evaluated each time when the participant provided the samples, the semen quality data were included in the final analyses regardless of whether the donation criteria were met. For those who did not meet the donation criteria, they were still enrolled in the study and requested to provide 1–4 additional semen samples at different time points (days 1–15, 16–31, 32–63, and ≥64 from initial recruitment) for further screening.

During the study period, different questionnaires were administrated at days of 1–15, 16–31, 32–63, and ≥64 from initial baseline recruitment via in-person interviews. Collected information included demographic factors (e.g., age, history of having ever fathered a pregnancy, education level, occupation, and household income), lifestyle habits (e.g., smoking status, alcohol consumption, tea consumption, and abstinence time), and physical examination results (e.g., height, weight, waistline, and hipline). The Pittsburgh Sleep Quality Index (PSQI) questionnaire was administered at 16–31 days (n = 752) and then again at ≥64 days (n = 560) from initial baseline recruitment; 470 men completed the PSQI questionnaire at both time periods.

Among the 1487 men who were enrolled, 102 men were excluded at baseline due to genetic or sexually transmitted diseases (e.g., syphilis, HIV, and hepatitis, etc.), 543 men did not complete the PSQI questionnaire in either of the two follow-up periods (16–31 and ≥64 days) due to a lack of time (n = 96) or due to the loss to follow-up (e.g., men who only attended the initial baseline screening; n = 447). Finally, a total of 842 participants completed at least one PSQI questionnaire and were included in our present analysis. This work was approved by the Ethics Committee of the Center for Reproductive Medicine, Tongji Medical College before the recruitment of participants. All participants signed informed consent forms at enrollment.

2.2. Assessment of sleep duration and sleep quality

Sleep duration (including total sleep duration, night sleep duration, and daytime napping duration) and sleep quality were evaluated by the PSQI questionnaire (Lu et al., 2014). Sleep quality was calculated as the sum score of 19 items in the PSQI: lower scores indicate better sleep quality with good sleep quality defined as a total PSQI score ≤5.0 (Buysse et al., 1989). The night sleep duration was the time interval between the self-reported time point of falling asleep and that of waking up (Chen et al., 2016). Daytime napping was assessed by asking “did you take a midday nap?” If participants answered “yes”, they were further asked about the usual duration of their midday nap. The total sleep duration was the sum of night sleep duration and daytime napping duration.

2.3. Assessment of semen quality

Men underwent a semen sample collection and examination on the same day as the PSQI was administrated on days 16–31 and then days ≥64 from initial baseline recruitment. However, men could also provide additional semen samples following these two time periods. Volunteers collected semen samples into sterile polypropylene containers by masturbation. After liquefaction, sperm volume, concentration, and motility were determined by trained laboratory technicians following the guidelines of the World Health Organization (WHO) (WHO, 1999), as previously described (Rao et al., 2015). Briefly, a weighing method assuming a density of 1.0 g/mL was utilized to estimate sperm volume. Sperm concentration was evaluated by placing 10 μL of well-mixed semen into a clean Makler chamber using an optical microscope. Total sperm count was calculated by multiplying sperm volume with concentration. Four motility parameters [i.e., fast progressive sperm (A), slow progressive sperm (B), non-progressive sperm (C), and immotile sperm (D)] were assessed using an ocular grid. Total motility was the sum of progressive and non-progressive motility (WHO, 2010). All semen determinations were performed by professional technicians using the same apparatus. Internal quality control was assessed each day to ensure that the within-day and between-day variations were < 10%. Among the 842 men included in our current analysis, 10% (n = 88) provided 2 semen samples, 17% (n = 145) provided 3, 13% (n = 110) provided 4, and 59% (n = 495) provided at least 5 (maximum: 27 specimens per subject).

2.4. Data analyses

Descriptive analysis was conducted to describe volunteers’ demographic characteristics, sleep duration/quality, and semen quality parameters. The differences in demographic characteristics between the whole population (n = 1487) and those included in (n = 842) and

excluded (n = 645) from our current analysis were assessed using Kruskal-Wallis test or chi-square tests where appropriate. Wilcoxon matched-pairs signed-ranks test was also used to compare the differences in total sleep duration, night sleep duration, daytime napping duration, and total PSQI score measured at two different time points. For men who completed the PSQI questionnaire more than once (n = 470), we used the arithmetic mean values in subsequent analyses.

Semen quality parameters were analyzed on a logarithmic scale to normalize the distribution. Intraclass correlation coefficients (ICCs) were calculated to assess the reproducibility of repeated measurements of semen quality (Rosner, 1999). The associations of categorical total sleep duration [< 6.0, 6.0– < 6.5, 6.5– < 7.0, 7.0– < 7.5, 7.5– < 8.0, 8.0– < 8.5 (reference), 8.5– < 9.0, and ≥9.0 h/day (h/d)], night sleep duration [< 6.0, 6.0– < 6.5, 6.5– < 7.0, 7.0– < 7.5, 7.5– < 8.0 (reference), 8.0– < 8.5, 8.5– < 9.0, and ≥9.0 h/d], daytime napping duration [no (0.0 h/d) and yes (> 0.0 h/d)], and sleep quality [good (≤5.0) and poor (> 5.0)] with repeated measures of semen quality parameters were evaluated using linear mixed-effects models with an individual-specific random intercept (Verbeke and Molenberghs, 2000). For results showing some evidence of an association, we further applied natural cubic spline functions to explore potential non-linear dose-response relationships (Bates et al., 2015). All models were adjusted for age (continuous), BMI (continuous), waist-hip ratio (continuous), abstinence time (continuous), history of having ever fathered a child (yes or no), education level (lower than undergraduate or undergraduate or higher), occupation (employed, unemployed, or student), smoking status (never, former, or current), alcohol consumption (never, former, or current), tea consumption (yes or no), household income (≤4000, 4001–8000, or > 8000 RMB Yuan/month), and sampling season (spring, summer, fall, or winter). In the analysis for total sleep duration, total PSQI score was also adjusted for in the mixed-effects models; night sleep duration, daytime napping duration, and total PSQI score were mutually adjusted for in models when examining the independent association.

To evaluate the influence of missing values, we finally re-analyzed the linear mixed-effects models by using the median imputation methods to handle missing data. To test the robustness of our results, we used the within-subject average sperm quality parameters as the outcome and analyzed associations with average sleep duration/quality using linear regression models. We also used either the first or second measured sleep variables as the exposures and separately analyzed the associations with repeated measures of semen quality parameters using linear mixed-effects models. Stata software version 15.0 (Stata Corp, College Station, Texas, USA) and R version 3.5.1 (https://www.r-project.org/) were used for all analyses.

3. Results

3.1. Participants' characteristics

Compared with the total cohort population (n = 1487) and participants included in the present analysis (n = 842), men that were excluded were more likely to be current smokers, and have less than a bachelor's degree (Table 1). No apparent differences were observed for other characteristics. Participants included in our current analysis had a mean [standard deviation, (SD)] age, body mass index (BMI), waist-hip ratio, and abstinence time of 28 (5.4) years, 23 (3.2) kg/m^2, 0.85 (0.056), and 6.2 (3.1) days, respectively. The majority of participants (71%) had never fathered a pregnancy, 523 (62%) had less than a bachelor degree, 496 (59%) were never smokers, 605 (72%) had alcohol consumption at least once over the past 3 months, and 588 (70%) had a self-reported household income of > 4000 RMB Yuan per month. Only 14% of the semen samples were collected during winter (Table 1).

3.2. Distribution of sleep duration and sleep quality

Sleep characteristics measured at two different time points [mean (SD) of the interval between the two-time points was 58 (38) d] are shown in Table S1 (supplemental material). There were no apparent differences in total sleep duration, night sleep duration, and daytime napping duration; however, the second-measurement total PSQI score was much lower than the first-measurement (1.9 vs. 2.5). Among participants, the mean (SD) values of total sleep duration, night sleep duration, daytime napping duration, and total PSQI score were 8.3 (1.0) h/d, 7.8 (0.94) h/d, 0.50 (0.52) h/d, and 2.3 (1.8), respectively (Table 2).

3.3. Distribution and variability of semen quality parameters

A total of 5601 semen specimens were collected among 842 men. Their mean (SD) values of sperm volume, concentration, total count, total motility, and progressive motility were 3.1 (1.3) mL, 59 (22) million/mL, 177 (92) million, 60 (12) %, and 57 (12) %, respectively (Table 2). Fair-to-good reproducibility was obtained for serial measures of sperm volume, concentration, and total count (ICC = 0.54, 0.62, and 0.50, respectively); for total and progressive motility, however, reproducibility was poor (ICC = 0.20 and 0.22, respectively) (Table 3).

3.4. Association of sleep duration and sleep quality with semen quality parameters

Compared with men reporting total sleep duration of 8.0 to 8.5 h/d, those who slept less than 6.0 h/d and higher than 9.0 h/d had lower sperm volume of 12% [95% confidence interval (CI): −22%, −0.68%; *p*-value = 0.039] and 3.9% (95% CI: −7.3%, −0.44%; *p*-value = 0.027), respectively; men who slept 6.0 to 6.5 h/d had lower total and progressive sperm motility of 5.1% (95% CI: −9.3%, −0.66%; *p*-value = 0.025) and 5.9% (95% CI: −10%, −1.2%; *p*-value = 0.015), respectively. No notable differences were observed for sperm concentration and total sperm count in relation to total sleep duration (Table 4). Compared with men reporting night sleep duration of 7.5 to 8.0 h/d, those who slept < 6.0 h/d had lower total and progressive sperm motility of 4.4% (95% CI: −8.4%, −0.24%; *p*-value = 0.038) and 5.0% (95% CI: −9.2%, −0.48%; *p*-value = 0.030), respectively. No clear associations were observed for other sperm parameters in relation to night sleep duration and daytime napping duration (Table 4). Compared with men who reported good sleep quality (total PSQI score ≤5.0), those who reported poor sleep quality (total PSQI score > 5.0) had lower total sperm count, total motility, and progressive motility of 8.0% (95% CI: −15%, −0.046%; *p*-value = 0.049), 3.9% (95% CI: −6.2%, −1.5%; *p*-value = 0.002), and 4.0% (95% CI: −6.5%, −1.4%; *p*-value = 0.003), respectively. Sleep quality was not associated with sperm volume or concentration (Table 4). These results were largely unchanged when we applied the median imputation method to handle missing data or used the within-subject average sperm quality parameters as the outcome (Tables S2–S3, supplemental material). We also separately assessed associations with either the first or second measured sleep variables in relation to semen quality; results were relatively unchanged (Tables S4–S5, supplemental material).

3.5. Dose-response association of sleep duration and sleep quality with semen quality parameters

Consistent with the results in our primary analysis, we observed an inverted U-shaped association between total sleep duration and sperm volume based on the cubic spline model: both shorter and longer total sleep duration was associated with decreased sperm volume (Fig. 1). Moreover, total and progressive sperm motility appeared to decrease monotonically with decreasing night sleep duration among participants

Table 1
Comparison of volunteers' characteristics [*n* (%) or mean ± SD].

Characteristics	Total cohort population (*n* = 1487)[a]	Men included in current analyses (*n* = 842)[b]	Men excluded from current analyses (*n* = 645)[c]	*p*-value
Age, years	28 ± 5.3	28 ± 5.4	28 ± 5.1	0.21
BMI, kg/m^2	23 ± 3.3	23 ± 3.2	23 ± 3.3	0.14
Waist-hip ratio	0.85 ± 0.056	0.85 ± 0.056	0.85 ± 0.056	0.93
Ever fathered a child				0.65
No	1074 (72)	599 (71)	475 (74)	
Yes	409 (28)	239 (28)	170 (26)	
Education level				0.04
Less than undergraduate	965 (65)	523 (62)	442 (69)	
Undergraduate or above	522 (35)	319 (38)	203 (31)	
Occupation status				0.29
Employed	1181 (80)	653 (78)	528 (82)	
Student	241 (16)	152 (18)	89 (14)	
Unemployed	65 (4.0)	37 (4.0)	28 (4.0)	
Smoking status				< 0.001
Never	789 (53)	496 (59)	293 (45)	
Current	590 (40)	287 (34)	303 (47)	
Former	108 (7.0)	59 (7.0)	49 (8.0)	
Alcohol consumption				0.39
Never	373 (25)	228 (27)	145 (22)	
Former	16 (1.0)	9 (1.0)	7 (1.0)	
Current	1098 (74)	605 (72)	493 (77)	
Regular (≥1 time/week)	189 (13)	95 (11)	94 (15)	
Occasional (< 1 time/week)	909 (61)	510 (61)	399 (62)	
Tea drinking				0.93
No	1069 (72)	602 (71)	467 (72)	
Yes	418 (28)	240 (29)	178 (28)	
Household income, RMB Yuan per month				0.82
≤4000	430 (29)	253 (30)	177 (28)	
4001–8000	561 (38)	308 (37)	253 (39)	
> 8000	494 (33)	280 (33)	214 (33)	
Abstinence time, days [d]	6.2 ± 3.4	6.2 ± 3.1	6.4 ± 5.0	< 0.001
Seasons [d]				0.45
Spring	1617 (25)	1354 (24)	263 (26)	
Summer	2298 (34)	1972 (35)	326 (32)	
Fall	1776 (27)	1487 (27)	289 (29)	
Winter	917 (14)	788 (14)	129 (13)	

Abbreviations: BMI, body mass index; SD, standard deviation.
[a] A total of 1 man had missing information on BMI, 1 on waist circumference, 4 on history of having ever fathered a child, and 2 on household income.
[b] A total of 4 men had missing information on history of having ever fathered a child, and 1 on household income.
[c] A total of 1 man had missing information on BMI, 1 on waist circumference, and 1 on household income.
[d] The numbers shown here are total numbers of donated sperm samples, and each participant provided repeated samples throughout the study period. The total number of sperm samples for the total cohort participants was 6608, and it was 5601 for those included in the analysis and 1007 for those excluded from the analysis.

Table 2
Distribution of sleep duration, sleep quality and semen quality parameters.

Measurements	*n*[a]	Arithmetic mean ± SD	Median (25th, 75th)
Sleep duration and quality			
Total sleep duration, h/d	842	8.3 ± 1.0	8.3 (7.8–8.9)
Night sleep duration, h/d	842	7.8 ± 0.94	7.8 (7.3–8.4)
Daytime napping duration, h/d	842	0.50 ± 0.52	0.45 (0.0–0.75)
Total PSQI score	835	2.3 ± 1.8	2.0 (1.0–3.0)
Semen quality parameters			
Semen volume, mL	5601	3.1 ± 1.3	2.8 (2.0–4.0)
Sperm concentration, million/mL	5601	59 ± 22	62 (45–70)
Total sperm count, million per ejaculate	5601	177 ± 92	166 (120–228)
Total motility, %	5601	60 ± 12	64 (54–67)
Progressive motility, %	5601	57 ± 12	60 (51–64)

Abbreviations: PSQI, Pittsburgh Sleep Quality Index; SD, standard deviation.
[a] A total of 7 men had missing information on total PSQI score.

who slept less than 7.8 h/d (median). Similarly, a decline in the total count, total motility, and progressive motility was observed among men reporting poor sleep quality (total PSQI score > 5.0) (Fig. 1).

4. Discussion

Among 842 healthy young men who provided repeated semen samples over a 6-month period, we found high variability in serial measures of total and progressive sperm motility, whereas fair-to-good reproducibility for sperm volume, concentration, and total count. Based on mixed-effects models that accounted for repeated measures of semen quality, we found that both too short and too long total sleep duration were associated with lower sperm volume; and too short night sleep duration was associated with lower total and progressive sperm motility. Men reporting poor sleep quality had a lower total count, total motility, and progressive motility compared with men reporting good sleep quality. These trends were confirmed in the restricted cubic spline models and were also robust to multiple sensitivity analyses.

Several studies have assessed the variability of semen quality parameters in subfertile men (Chiu et al., 2017; Francavilla et al., 2007), healthy men (Poland et al., 1986), and sperm donors (Keel, 2006). Consistent with our findings, these studies all reported that repeated measures of sperm volume, concentration, and total count were relatively stable within individuals (ICCs = 0.64–0.98). The reproducibility of sperm motility in these studies was uniformly lower than the other sperm parameters but remained fair-to-excellent (ICCs = 0.51–0.96), which is much higher than our present results (ICCs = 0.20 and 0.22, respectively). Discrepancies between our

Table 3
The variance apportionment of repeated semen quality parameters (log-transformed) collected from 842 men (n = 5601).

Semen quality parameters	Variance component		ICC (95% CI)
	Between-person σ^2 (%)	Within-person σ^2 (%)	
Semen volume, mL	0.026 (54%)	0.022 (46%)	0.54 (0.51, 0.57)
Sperm concentration, million/mL	0.049 (62%)	0.030 (38%)	0.62 (0.59, 0.65)
Total sperm count, million per ejaculate	0.068 (50%)	0.068 (50%)	0.50 (0.47, 0.54)
Total motility, %	0.0042 (20%)	0.017 (80%)	0.20 (0.17, 0.23)
Progressive motility, %	0.0052 (22%)	0.018 (78%)	0.22 (0.19, 0.25)

Abbreviations: σ^2, variance; CI, confidence interval; ICC, intraclass correlation coefficient.

present results and prior studies may be attributed to differences in abstinence duration (6.2 d vs. 3 d) (Chiu et al., 2017; Leushuis et al., 2010). Previous studies have shown that longer abstinence duration was associated with decreasing sperm motility (Blackwell and Zaneveld 1992; De Jonge et al., 2004; Mayorga-Torres et al., 2015; Sauer et al., 1988), which may have resulted in greater variability in sperm motility. The differences in population characteristics and study design may also lead to variation in estimated ICCs. Our recruited volunteers were relatively homogeneous (well-educated healthy men aged between 22 and 45 years), which may have reduced the contribution of between-individual variance to the total variance.

Several studies have investigated the association of sleep duration with human semen quality (Chen et al., 2016; Liu et al., 2017; Shi et al., 2018), but results were inconsistent. In our present study, we revealed an inverse U-shaped association between total sleep duration and sperm volume based on the cubic spline models, which is consistent with findings among 796 college students who provided two semen samples at different time points (Chen et al., 2016). However, Chen et al. (2016) also found an inverse U-shaped association between sleep duration and total sperm count. In contrast, Shi et al. (2018) found a monotonously positive association between sleep duration and sperm concentration among 328 men who underwent semen examination; Liu et al. (2017)

Table 4
Percentage change (95% CI) in semen quality parameters associated with average sleep duration and quality based on mixed-effects models (n = 5554).[a]

Variables	n	Semen volume, mL	Sperm concentration, million/mL	Total sperm count, million per ejaculate	Total motility, %	Progressive motility,%
Total sleep duration, h/d[b]						
< 6.0	86	−12 (−22, −0.68)*	13 (−4.3, 33)	−1.1 (−19, 21)	−1.2 (−6.7, 4.6)	−1.6 (−7.4, 4.7)
6.0− < 6.5	83	−1.8 (−11, 7.9)	−2.8 (−14, 10)	−4.0 (−18, 12)	−5.1 (−9.3, −0.66)*	−5.9 (−10, −1.2)*
6.5− < 7.0	154	−1.7 (−8.2, 5.4)	−3.2 (−12, 6.2)	−4.8 (−15, 6.5)	0.63 (−2.7, 4.1)	0.45 (−3.2, 4.2)
7.0− < 7.5	655	−1.0 (−5.3, 3.5)	−1.2 (−6.9, 4.8)	−2.2 (−9.0, 5.1)	0.77 (−1.3, 2.9)	0.64 (−1.6, 2.9)
7.5− < 8.0	1047	−1.6 (−5.3, 2.1)	3.9 (−1.2, 9.2)	2.0 (−4.0, 8.5)	1.1 (−0.65, 3.0)	1.2 (−0.70, 3.2)
8.0− < 8.5 (Ref)	1324	0.00	0.00	0.00	0.00	0.00
8.5− < 9.0	938	−1.4 (−5.1, 2.3)	0.14 (−4.8, 5.3)	−1.3 (−7.2, 4.9)	0.43 (−1.4, 2.3)	0.48 (−1.5, 2.4)
≥9.0	1267	−3.9 (−7.3, −0.44)*	0.27 (−4.4, 5.2)	−3.6 (−9.1, 2.1)	0.64 (−1.1, 2.4)	0.56 (−1.3, 2.4)
Night sleep duration, h/d[c]						
< 6.0	152	−6.7 (−15, 2.2)	−1.7 (−13, 11)	−7.6 (−20, 7.2)	−4.4 (−8.4, −0.24)*	−5.0 (−9.2, −0.48)*
6.0− < 6.5	202	1.6 (−4.9, 8.6)	3.5 (−5.3, 13)	5.2 (−5.6, 17)	0.41 (−2.8, 3.7)	0.27 (−3.1, 3.8)
6.5− < 7.0	430	0.37 (−4.4, 5.4)	−4.7 (−11, 1.7)	−4.4 (−12, 3.6)	−0.49 (−2.8, 1.9)	−0.62 (−3.1, 1.9)
7.0− < 7.5	1091	−0.27 (−3.8, 3.4)	−1.3 (−6.0, 3.7)	−1.6 (−7.2, 4.5)	0.49 (−1.2, 2.3)	0.38 (−1.5, 2.3)
7.5− < 8.0 (Ref)	1448	0.00	0.00	0.00	0.00	0.00
8.0− < 8.5	1067	0.80 (−2.8, 4.6)	−3.9 (−8.5, 1.0)	−3.0 (−8.7, 3.0)	−0.42 (−2.1, 1.3)	−0.36 (−2.2, 1.5)
8.5− < 9.0	569	−1.8 (−6.0, 2.5)	−2.9 (−8.3, 2.9)	−4.6 (−11, 2.4)	0.24 (−1.8, 2.4)	0.0 (−2.2, 2.3)
≥9.0	595	−2.7 (−6.9, 1.7)	−1.2 (−6.8, 4.8)	−3.8 (−10, 3.3)	0.43 (−1.7, 2.6)	0.43 (−1.8, 2.7)
Daytime napping duration, h/d[d]						
No (0.0 h/d)	1584	0.00	0.00	0.00	0.00	0.00
Yes (> 0.0 h/d)	3970	2.2 (−0.42, 5.0)	1.6 (−2.0, 5.2)	3.9 (−0.45, 8.5)	0.27 (−1.0, 1.6)	0.35 (−1.0, 1.7)
Sleep quality[e]						
Good (≤5.0)	5218	0.00	0.00	0.00	0.00	0.00
Poor (> 5.0)	336	−1.9 (−6.8, 3.2)	−6.3 (−13, 0.26)	−8.0 (−15, −0.046)*	−3.9 (−6.2, −1.5)*	−4.0 (−6.5, −1.4)*

Abbreviations: BMI, body mass index; CI, confidence interval; Ref, reference. *P < 0.05.

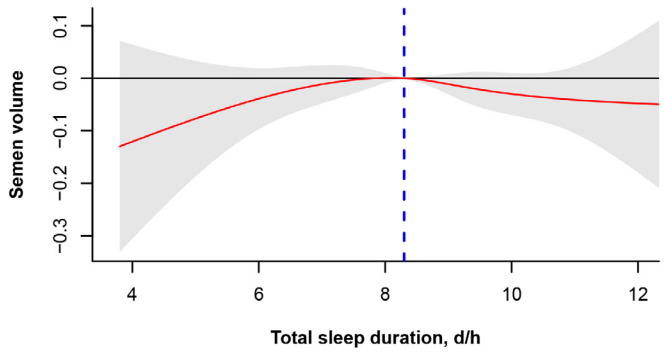
[a] A total of 20, 5, and 22 missing information on history of having ever fathered a child, household income, and sleep quality score, respectively. Regression coefficients (95% CI) were converted into percentage change (95% CI) using the following formula: {[exp(beta) − 1] × 100}. All models were adjusted for age (continuous), BMI (continuous), waist-hip ratio (continuous), abstinence time (continuous), history of having ever fathered a child (yes or no), education level (less than undergraduate or undergraduate or above), occupation (employed, unemployed, or student), smoking status (never, former, or current), alcohol consumption (never, former, or current), tea consumption (yes or no), household income (≤4000, 4001–8000, or > 8000 RMB Yuan/month), and sampling season (spring, summer, fall, or winter).

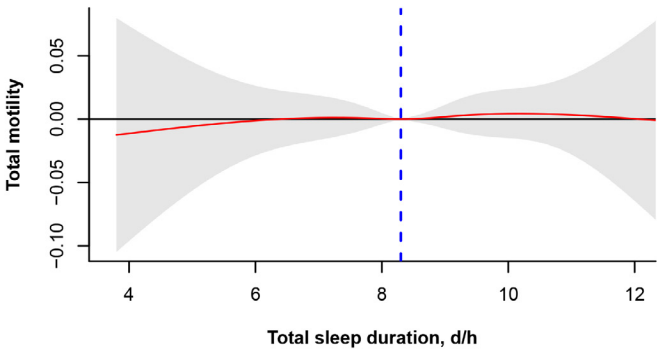
[b] Additionally adjusted for total PSQI score (continuous).

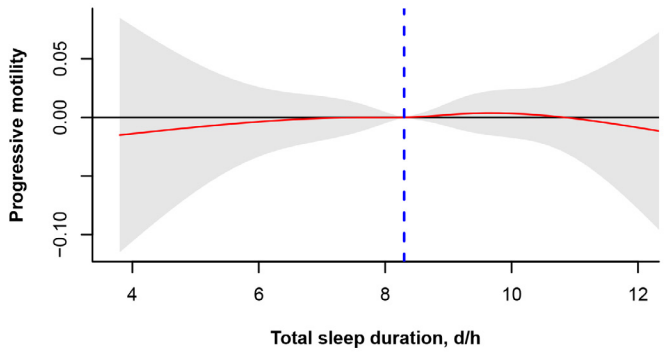
[c] Additionally adjusted for daytime napping duration (continuous) and total PSQI score (continuous).

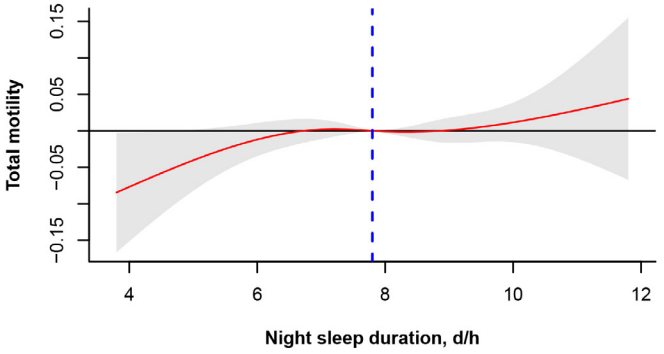
[d] Additionally adjusted for night sleep duration (continuous) and total PSQI score (continuous).

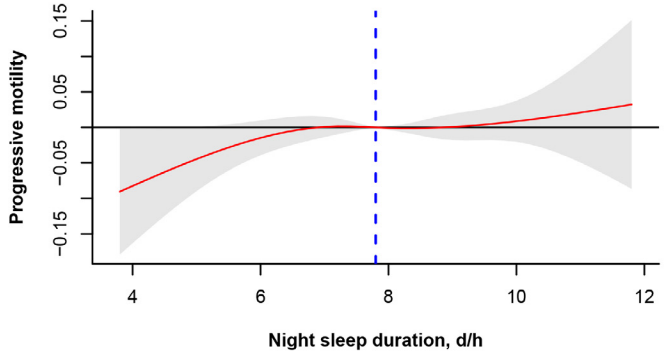
[e] Additionally adjusted for night sleep duration (continuous) and daytime napping duration (continuous).

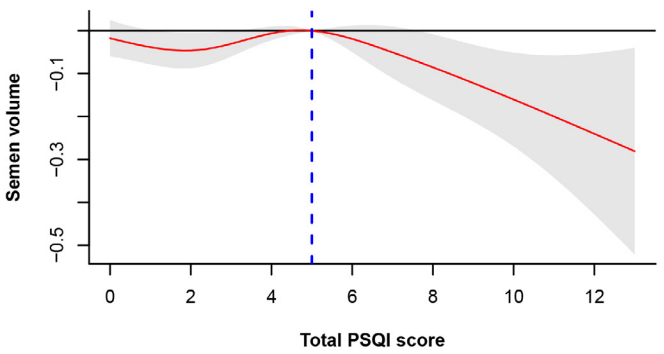


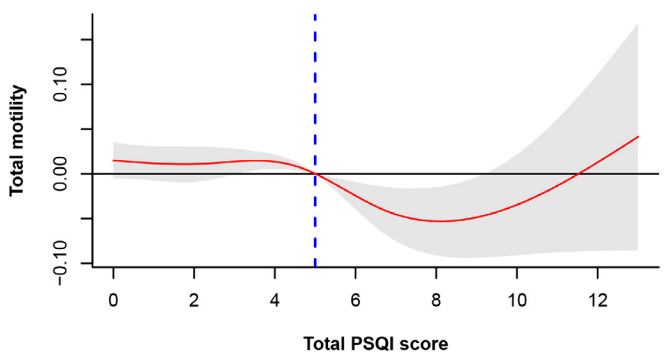












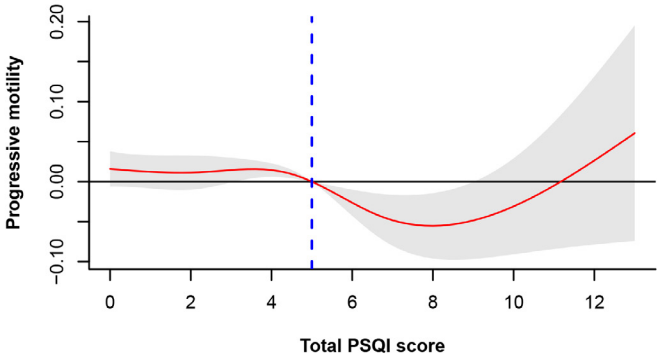


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Fig. 1. Dose-response relationships of sleep duration and quality with semen quality parameters (log-transformed) based on natural cubic spline models (n = 5554). [a] Abbreviations: BMI, body mass index; PSQI, Pittsburgh Sleep Quality Index. [a] A total of 20, 5, and 22 missing information on history of having ever fathered a child, household income, and sleep quality score, respectively. The reference values (i.e., the blue vertical dotted lines) were set to 8.3 h/d (median), 7.8 h/d (median), 0 h/d, and 5 for total sleep duration, night sleep duration, daytime napping duration, and total PSQI score, respectively. The black horizontal solid lines were set to "0". The red solid lines represent the effect estimates, and the shadowed parts represent the 95% CIs. All models were adjusted for age (continuous), BMI (continuous), waist-hip ratio (continuous), abstinence time (continuous), history of having ever fathered a child (yes or no), education level (less than undergraduate or undergraduate or above), occupation (employed, unemployed, or student), smoking status (never, former, or current), alcohol consumption (never, former, or current), tea consumption (yes or no), household income (≤4000, 4001–8000, or > 8000 RMB Yuan/month), and sampling season (spring, summer, fall, or winter). In the analysis for total sleep duration, total PSQI score was also adjusted for in the mixed-effects models; night sleep duration, daytime napping duration, and total PSQI score were mutually adjusted for in models when examining the independent association.

revealed that both short and long sleep duration were associated with decreased sperm count, survival rate, or motility among 981 healthy men. In contrast, we found that short sleep duration was associated with lower total and progressive sperm motility. The inconsistent results between studies may be related to the differences in study design, the composition of the recruited population, and, perhaps most importantly, the number of semen samples per subject to reflect individual semen quality over time. Similarly, Wise et al. (2018) found a U-shaped association between sleep duration and fecundability, a marker of couple-based fertility among healthy men in a North American preconception cohort. In the present study, we found a moderate-to-high within-individual variability in sperm motility, volume, concentration, and total count over months (ICCs = 0.20–0.62), indicating that a single measure of semen quality can result in measurement error and further bias risk estimation.

Growing evidence indicates that sleep quality is also a valuable measure of sleep (Bin 2016; Watson et al., 2015). To date, however, few studies have investigated the association between sleep quality and human semen quality. In support of our findings, Jensen et al. (2013) reported an inverse association between sleep disturbance and sperm concentration, total count, and percent of normal morphology among 953 healthy Danish men; Viganò et al. (2017) reported a lower semen volume among 382 Italian males who had difficulty in initiating sleep. However, it should be noted that the number of participants who had poor sleep quality in our study was relatively small (n = 54), which may have been insufficient to generate precise estimations. Further studies with sufficient sample size are needed to explore the joint associations of sleep duration and quality with semen quality.

The mechanisms underlying the associations of sleep duration and quality with semen quality remain unclear. Previous evidence has shown that both long and short sleep duration were associated with increased risk of obesity (Sermondade et al., 2013), decreased daytime testosterone levels (Leproult and Van Cauter 2011), and disrupted activity of enzymes related to sperm apoptosis (e.g., nitric oxide synthase and endothelial nitric oxide synthase) (Middendorff et al., 1997; O'Bryan et al., 2000), eventually leading to impaired male reproductive health. Similar to the mechanisms related to sleep duration, previous studies have also shown that poor sleep quality was associated with perturbations in the circadian rhythm (Luboshitzky et al., 2001), decreased serum testosterone levels (Monder et al., 1994), and impaired Sertoli cells in the seminiferous tubules (Choi et al., 2016).

The major strength of this study was that we obtained repeated measures of semen quality parameters per subject at multiple time points, which reduced measurement error. Additionally, our study volunteers were healthy men screened as potential sperm donors, who are more representative of reproductive-aged men compared to previous studies recruiting participants from infertility clinics (Viganò et al., 2017), college students (Chen et al., 2016), and military fitness examination (Jensen et al., 2013); however, cautions should still need to be taken when generalizing our findings to the general populations given that men with infertility problems were more likely to be underrepresented in the study samples. However, our study also has several limitations. First, sleep duration and sleep quality were self-reported; measurement error cannot be fully excluded. Nevertheless, 56% of the participants completed the PSQI questionnaire more than once during the study period, and arithmetic mean values were adopted to reduce measurement error. Second, the number of participants who had too short or long sleep duration and poor sleep quality in our study was relatively small, which limited our capacity to generate precise estimations. Third, although we have accounted for various potential confounders, unmeasured confounding may still influence our results. For instance, it is possible that both insufficient and long sleep duration may be associated with mental health problems, including anxiety and depression (Liu et al., 2013; Wise et al., 2018), which may affect sperm quality and potentially the probability of pregnancy (Nillni et al., 2016). However, our study included generally healthy men who voluntarily donated semen samples and it is thus unlikely that men with severe mental health problems would participate in the study and the results were affected. Finally, similar to many other observational studies, causality cannot be inferred from our present study.

5. Conclusions

In conclusion, using repeated measurements of semen quality parameters, we found that short or long sleep duration and poor sleep quality were associated with impaired semen quality. The high within-individual variability of total and progressive sperm motility suggests that collection of repeated semen samples is needed to reduce classification error. Given the growing evidence of a global decline in human semen quality and the increasing prevalence of short sleep duration and poor sleep quality, additional research is needed to confirm our findings and explore potential underlying mechanisms using a repeated measurement design.

CRediT authorship contribution statement

Heng-Gui Chen: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing - original draft, and Writing - review & editing. **Bin Sun:** Investigation, Validation, and Writing - review & editing. **Ying-Jun Chen:** Investigation, Validation, and Writing - review & editing. **Jorge E. Chavarro:** Methodology and Writing - review & editing. **Si-Heng Hu:** Methodology, Supervision, and Writing - review & editing. **Cheng-Liang Xiong:** Funding acquisition, Resources, Supervision, and Writing - review & editing. **An Pan:** Conceptualization, Funding acquisition, Project administration, Resources, Supervision, and Writing - review & editing. **Tian-Qing Meng:** Conceptualization, Funding acquisition, Project administration, Resources, Supervision, and Writing - review & editing. **Yi-Xin Wang:** Conceptualization, Funding acquisition, Project administration, Resources, Supervision, and Writing - review & editing. **Carmen Messerlian:** Conceptualization, Methodology, and Writing - review & editing.

Declaration of Competing Interest

The authors declare they have no actual or potential competing financial interests.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2019.105368.

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