Sleep and Sleep Disorders During Pregnancy and Postpartum:

The Life-ON Cohort Study

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Key points

Question: What is the prevalence and course of sleep disorders across pregnancy and postpartum?

Findings: In this cohort study, insomnia was the most prevalent sleep disorder peaking just after delivery, especially in elder pluriparous women; EDS was second, peaking in early pregnancy, RLS was the third one and peaked in late pregnancy. Obstructive sleep apnea in mid pregnancy was infrequent and correlated with BMI.

Meaning: Sleep disorders are highly represented and distributed differently across pregnancy and puerperium, requiring attention by gynecologists, who should always screen for sleep complains and share significant cases with a sleep expert for an appropriate diagnostic and therapeutic work-up.

Abstract

Importance: sleep disorders are frequent during pregnancy and puerperium and contribute to the development of several complications. However, objective polysomnographic (PSG) studies and longitudinal sleep assessments are few and often limited in scope.

Objective: to prospectively assess sleep and sleep disorders during pregnancy and postpartum in a large cohort of women.

Design: first data release from the prospective Life-ON study, including home polysomnography between the 23rd and 25th week of pregnancy and sleep-related questionnaires at 11 points in time during pregnancy and one year postpartum, between 2016 and 2020.

Setting: multicenter, prospective study, recruiting consecutive pregnant women from the local hospital gynecological departments.

Participants: pregnant women between 18 and 55 years of age and without major morbidities, were recruited at a gestational age between 10 to 15 weeks by four sleep centers in Italy and Switzerland.

Main Outcome measures: frequency and course of daytime sleepiness, insomnia, low quality of sleep, restless legs syndrome, sleep breathing and periodic limb movements (PLMS) across pregnancy and puerperium. Correlation between symptoms and demographic and PSG measures.

Results: 439 pregnant women (mean age 33.7 ±4.2 yrs) were enrolled, with full-night PSG data available for 353 women. Poor quality of sleep was reported by 34% of women in the first trimester

of pregnancy, by 46% of women in the third trimester, and by as many as 71% of women in the first month after delivery. A similar trend was seen for insomnia. Excessive daytime sleepiness peaked in the first trimester (30% of women), and decreased in the third trimester, to 22% of women. Prevalence of RLS during pregnancy was 27%, with a peak in the third trimester. Sleep-disordered breathing had a prevalence of 4.2% and correlated positively with BMI. A PLMS index larger than 4 was found in 55% of women. PSG data revealed that24% of women slept less than 6 hours, and 30.6% of women had a sleep efficiency below 80%.

Conclusions

The Life-ON study provides the largest PSG dataset coupled with longitudinal subjective assessments of sleep quality in pregnant women to date. Sleep disorders are highly frequent and distributed differently during pregnancy and postpartum. Routine assessment of sleep disturbances in the perinatal period is necessary to improve early detection and clinical management.

Introduction

Sleep and pregnancy are reciprocally linked, with pregnancy inducing changes in sleep and related disorders, and sleep disorders affecting pregnancy and its outcome. Sleep disturbances are known to be very common during pregnancy[1] and the postpartum period.[2] More than 40% of pregnant women report poor sleep quality and reduction of total sleep time.[3] Daytime sleepiness seems to be particularly frequent in the first trimester of pregnancy, while insomnia appears to be more common in the third trimester, together with restless legs syndrome (RLS) and sleep apnea.[4] Insomnia and RLS are known to increase the risk of perinatal depression (PND).[5] Obstructive sleep apnea (OSA) is a risk factor for gestational hypertension[2] and affects fetal growth and APGAR score at birth[6]. While cross-sectional studies of subjectively reported sleep-related symptoms have been described in the literature, available results depend on the time of gestation and on the objectivity of assessment tools used.[3] Although polysomnographic (PSG) studies provide accurate information about sleep, their use is limited by feasibility and costs involved. As a consequence, prospective sleep studies are few, and generally limited in size and scope[7].

In this study, we aimed to characterize sleep and assess the frequency of major sleep disorders during pregnancy and 6 months postpartum, from a large prospective cohort.

Methods

Data collection

The presented results derive from the prospective multicenter Life-ON Study (Perinatal Depression: Chronobiology, Sleep related Risk Factors and Light Therapy, 320030_160250 / 1); details on the complete study protocol have previously been published.[8]

The Life-ON study aimed to identify sleep-related risk factors for perinatal depression. A large, naturalistic, consecutive cohort of pregnant women was recruited by four sleep centers, in Bologna, Milan and Turin (Italy) and in Lugano (Switzerland), and followed up to one year after delivery. All women gave written informed consent to participate in the study and the study was approved by local ethical committees.

The inclusion criteria for the study were: age between 18 and 55 years, lack of major medical conditions, and gestational age between 10 to 15 weeks at the time of inclusion. Exclusion criteria were: any psychiatric diagnosis, recent or current use of psychotropic drugs (within the last 6 months), and intrauterine fetal death.

Participating women underwent eleven scheduled visits, three of which were face-to-face (one per trimester of pregnancy) and eight were either face-to-face visits or telephone conversations during twelve months postpartum (Table 1). Participants were examined by a multidisciplinary team of gynecologists, psychologists, psychiatrists, and neurologist experts in sleep medicine.

Sleep Questionnaires and Reporting Scales

Sleep quality was assessed by the Pittsburgh Sleep Quality Index (PSQI): a self-administered 18-item questionnaire with scores ranging between 0 and 21, where a score higher than or equal to 5 identifies poor-quality sleep.[9]

The presence and severity of insomnia were assessed by the Insomnia Severity Index (ISI): a self-administered 7-item questionnaire with scores ranging between 0 and 28, where a score between 8 and 14 identifies subthreshold insomnia, a score between 15 and 21 moderate insomnia, and scores higher than 21 severe insomnia.[10]

Daytime sleepiness was assessed by the Epworth Sleepiness Scale (ESS): a self-administered 8-item questionnaire with scores ranging between 0 and 24, where scores higher than 10 identify pathological sleepiness.[11]

The presence of restless legs syndrome (RLS) was assessed in a face-to-face interview. Women fulfilling the five standard diagnostic criteria for RLS[12] were classified as affected and were further assessed to quantify the severity of their symptoms using the International RLS Study Group Rating Scale (IRLS).[13]

Polysomnography

With each participant, a full night home polysomnography (PSG) was conducted, between the 23rd and 25th gestational week. The following parameters were monitored: electroencephalogram, electro-oculogram, electromyogram of submentalis and bilateral tibialis anterior muscles, electrocardiogram, airflow, thoracic and abdominal efforts, oxygen saturation, body position and microphone. Sleep and related events were first scored by a sleep specialist per center, and then centrally and blindly reviewed by a single sleep specialist (SR, neurologist), following standard guidelines.[14]

Statistical Analysis

In data processing, no imputation of missing values was performed. All women were a priori included in the analyses and only excluded from specific computations whenever one of the variables under focus was missing. The demographic characteristics of the group of women who completed the study were compared against those of the group of women who had dropped out, and differences were tested for significance using the *t*-test for age and BMI, and the Pearson's chi-square test for educational levels and smoking habits. The *t*-test was used also for testing differences in the ISI, PSQI and ESS indexes between parity groups and between age groups. Spearman’s rank-correlation coefficient was used for testing significance of pairwise correlations between variables. All statements of significance are based on a significance level of 0.05.

Results

Four hundred and thirty-nine pregnant women (age: mean = 33.7 yrs, std = 4.2) were recruited. The present paper provides data collected up to 6 months after pregnancy, when 299 (68.1%) women were still regularly followed, while 140 (31.9%) had dropped out. No significant differences in demographic characteristics (Table 2) were found between the women who completed the study and the women who dropped out (with $p = 0.76$ for age, $p = 0.34$ for BMI at visit 1, $p = 0.10$ for educational level, and $p = 0.48$ for smoking).

Sleepiness

Excessive daytime sleepiness (EDS) was reported by 46.9% women; these women had an ESS score higher than 10 in at least one of the 9 visits. During pregnancy, EDS was reported at least once by 40.7% of women. The mean of the ESS scores was highest in the first trimester of pregnancy (figure 1, *top left*), with 30.3% of women reporting a score higher than 10. Except for a transient plateau around delivery, sleepiness decreased over time, to 13.0% at visit 8 and 9.8% at visit 9.

EDS (ESS) correlated with insomnia (ISI) and with poor sleep quality (PSQI) with correlation coefficients for the PSQI ranging from 0.1 to 0.27 (p-value<0.005) and from 0.2 to 0.39 (p-value>0.005) for the ISI score (supplementary efigure 1). Moreover the Spearman rank correlation coefficient of the ESS and ISI scores averaged over all six visits was $r = 0.362$ ($p < 0.005$) and the correlation coefficient of the average ESS and PSQI scores was $r = 0.241$ ($p < 0.005$). Only women without missing values for both ISI and EES, and, respectively, ESS and PSQI were included in these analyses. No significant correlation was found of daytime sleepiness at visit 2 with respiratory disturbance (RDI) ($r = 0.038$, $p = 0.492$), nor with PLMS ($r = 0.0015$, $p = 0.978$).

Daytime sleepiness is present similarly in pluriparous and in primiparous women (supplementary efigure 2). A negative correlation was found between ESS and age, which was only significant in the period immediately following delivery, ie visit 5 (supplementary efigure 3 and 7); at this visit, women older than 37 years of age showed significantly lower ESS scores on average than younger women (p = 0.0041) .

Quality of Sleep and Insomnia

Figure 1 (*bottom left*) shows the trend of sleep quality (PSQI) and that of insomnia (ISI) (*top right*) throughout pregnancy and the puerperium. Both mean scores peaked around the time of delivery.

Sleep quality was judged to be poor by 33.7% of women in the first trimester of pregnancy, with this percentage increasing to 34.7% and 46.2% in the second and third trimesters respectively. Three weeks after delivery (visit 5), the mean of the observed PSQI scores peaked, with poor sleep quality for 71.4% of the women, which remained poor for almost half of the sample up to visit 9. Eighty-two percent of women had a PSQI score of 5 or above in at least one of the visits. Sleep quality was worse in pluriparous women than in primiparous (Figure 2, *bottom left*) and showed a positive correlation with age which was only significant at visit 2. (supplementary efigure 4).

The mean ISI score followed similar trends, with insomnia peaking in the third trimester of pregnancy (31.5%), and immediately after delivery (34.4%) (figure 1 (top right)). The percentage of women experiencing insomnia dropped to 15.9% 7 weeks after delivery. 247 women (56.3%) indicated insomnia at least once in visits 1 to 9. Insomnia was found to correlate positively with sleep quality, with correlation coefficients between the ISI and PSQI scores ranging from r = 0.650 at visit 5 to r = 0.752 at visit 3, with p-values<0.005 (supplementary efigure 5).

The ISI score neither correlated with the RDI score (correlation coefficient r = 0.0639, with p = 0.25) nor with PLMS (r = 0.0886, p = 0.11). Insomnia was significantly more represented among pluriparous women than among primiparous women (supplementary efigure 2), with $p = 0.0325$ at visit 1 and $p = 0.019$ at visit 2. Insomnia and age showed a positive correlation, yet without reaching statistical significance (supplementary efigure 6).

Restless Legs Syndrome

Figure 1 (*bottom right*) shows the trend of RLS occurrence, which peaked during the second and third trimesters of pregnancy. Around delivery, RLS prevalence dropped and reduced to 5.7% by visit 9. RLS was experienced in at least one of the visits 1 to 3 during pregnancy by 25% of women. The percentage of women experiencing RLS during their current pregnancy for the first time at visit 1, was 12.1%, while 13.7% had received a previous diagnosis of RLS. Among the women presenting with RLS at visit 1, 2.0% had mild RLS, 51.0% had moderate RLS, and 9.8% had severe or very severe RLS. These percentages were 3.8%, 50.9% and 18.9% during the 3rd trimester of pregnancy.

Polysomnographic Data

Table 3 reports the summary statistics of the polysomnographic data obtained from 353 women who underwent home recordings. Sleep macrostructure was basically preserved (supplementary efigure 8). The sleep stage percentages were similar across the four centers (supplementary efigure 9). 24.6% of women slept less than six hours, 41.4% of women more than 7 hours, and 9.9% slept more than 8 hours. The mean sleep efficiency was 83.0% (std 10.6%), with 30.0% of women having an SE lower than 80%. The mean latency of sleep to N1 was 16.8 minutes (std 18.4), with 28.3% of women having a latency longer than 20 minutes. Sleep proved fragmented: the mean number of awakenings was 24.0 (std 8.9), the mean number of arousals per hour was 12.2 (std 4.3), and the mean time of wakefulness after sleep onset (WASO) was 65.5 minutes (std 45.9).

Sleep Disordered Breathing

Sleep disordered breathing (SDB), defined by an RDI score of at least 5, was found in 15 (4.2%) women; 99.7% of them had mild SDB, 0.3% suffered from moderate SDB ($15 \leq RDI < 30$), and none had severe SDB ($RDI \geq 30$). The women with SDB had mostly obstructive hypopneas and respiratory-effort related arousals (RERA). These events were poorly associated with desaturations (mean ODI of 6.52 with std of 3.46 and mean SaO_2 of 94.5%, std 11.6%, in women with $RDI \geq 5$). Averaged over all women, the mean AHI in supine position was 2.2 (std 3.7), and the mean AHI in non-supine position was 0.9 (std 1.5). The mean AHI in REM over all women was 5.2 (std 6.9), and the mean AHI in NREM was 0.5 (std 1.1). The 15 women with an $RDI \geq 5$ had a mean AHI of 8.61, a mean AHI supine of 11.9, and a mean AHI in REM of 28.3. Averaged over all women, the mean time spent in supine position was 37.4% (std 0.22%); this percentage was 43.6% (std 0.24%) for women with $AHI \geq 5$. The RDI score correlated positively with the BMI (correlation coefficient $r = 0.253$, with $p < 0.005$) (Figure 2).

Periodic limb movements

Periodic limb movements during sleep (PLMS) were frequent in our study, with a mean PLMS index of 10.5 (std 17.3). 45% of women had a PLMS index higher than 5, 22.4% an index over 15, and 8.5% an index over 30. 31% percent of the women with a PLMS index equal or over 15 were also affected by RLS during pregnancy, while this percentage was 10% among the women with a PLMS index smaller than 15 ($p < 0.005$).

Discussion

In the Life-ON Study, prospective data on sleep were collected from 439 pregnant women during pregnancy and one-year postpartum, together with the largest collection of polysomnographies in pregnant women to date.

A generally poor quality of sleep was found in our naturalistic cohort during pregnancy and the first six months postpartum, with a progressive increase of PSQI scores. A recent meta-analysis showed that 45.7% of pregnant women had a PSQI score of at least 5 (mean PSQI score 6.07).[3] Longitudinal studies have shown mean PSQI scores to increase by 1.68 from the second to the third trimester, with gestational age being a significant moderator of heterogeneity. Our findings confirm these meta-analytic results and suggest age and parity status as risk factors for poor sleep quality.

A similar trend was observed in our study for insomnia, which was found in over 30% of women across the third trimester and immediate post-delivery period. From the literature, insomnia appears among the most prevalent sleep disorders during pregnancy, with rates ranging from 20% to 70% of women and increasing across pregnancy[15]. Unlike the previous literature, our findings suggest the poorest sleep quality and the highest peak of insomnia do not occur during pregnancy but rather immediately after delivery.

More than 45% of the women in our study reported EDS during their pregnancy, with a peak in the first trimester, followed by a reduction over time, of both the mean reported score and the prevalence, which normalized 6 months after delivery. While daytime sleepiness was found to correlate positively with insomnia and sleep quality, no correlation with parity status, RDI or PLMS was found. This finding suggests that other factors than clearly identifiable sleep disorders govern daytime sleepiness in early pregnancy. Facco *et al.* estimated the prevalence of EDS (defined as ESS > 10) at 32% and 38% in the 13th and 30th week of pregnancy respectively and, hence, did not describe a reduction in prevalence across pregnancy[16]. In a large cross-sectional study, Mindell *et al*. also did not find a significant change in prevalence of EDS (as ESS ≥ 10) across pregnancy, with percentages of EDS ranging between 43% and 51%[17]. In a study of 100 women in late pregnancy, Sarberg *et al*. found a prevalence of EDS (also as ESS ≥ 10) of 42%, without any correlation of EDS with snoring or AHI[18]. No solid prospective findings on EDS in the first year postpartum are available from the literature.

In our study, the overall prevalence of RLS during pregnancy was found to be 25%, with peaks in the second and third trimesters. This finding is in agreement with two studies on the occurrence of RLS in comparable populations of pregnant women in Northern Italy. Esposito *et al*.[19], reported a 20.4% prevalence of RLS, and Manconi *et al*. found a prevalence of 26% in the same geographic area.[20] Half of our women had suffered from similar symptoms previously in their life, without being pregnant. This finding supports the hypothesis that a genetic predisposition plays an important role in pregnancy-related RLS[21]. In our study group, around 19% of the RLS-positive women graded their symptoms in late pregnancy as "severe" or "very severe". The common view that RLS during pregnancy is usually mild may thus need some revision. These results, combined with the associated high risk of future idiopathic RLS and with the described correlation between pregnancy-related RLS and PND, support active dissemination of knowledge and distribution of existing guidelines for RLS management during pregnancy to all gynecologists.[22]

PLMS was a frequent finding in our study group, considering the young age and gender of the subjects involved: in the general population, PLMS is known to increase with age and is predominant in males. As expected, RLS correlated significantly with PLMS. The very few studies assessing PLMS during pregnancy did not report differences or just a mild increase of PLMS, when comparing pregnant to non-pregnant women[7].

Sleep macrostructure was essentially preserved in our study group, with a tendency towards a fragmentation and a decreased SE and TST. Previous available PSG data from pregnant women are based on very few studies on smaller samples. The largest available study was reported by Izci-Balserak *et al*., who obtained recordings from 123 women in the first trimester of their pregnancy and from 97 women in the third trimester[23]. There are no consistent studies known in which a PSG was performed in the same period of pregnancy as ours[7].

Polysomnographic data on sleep-related breathing abnormalities in (healthy) pregnant women are scarce and divergent. If non-polysomnographic studies are considered, SDB is frequently reported during pregnancy, with a prevalence ranging between 12% and 32%, depending on its definition. Izci-Balserak *et al*. found a prevalence of OSA (AHI > 5) of 14% and 26% in the first and third trimesters, which was substantially lower (4.2%) in our larger cohort. These dissimilarities are probably due to differences in BMI in early pregnancy, which was relatively lower in our sample (23 vs 30 on average), and to a different pregnancy week of assessment.

The main limitations of our study are the lack of a control group of non-pregnant women and of postpartum follow-up polysomnographies. . The strengths on the other hand are the prospective analysis of non-PSG data, the combination of subjective and objective data, and the size and homogeneity of the Life-ON study group.

In conclusion, EDS appears to prevail in the first trimester of pregnancy, whereas insomnia and an overall low quality of sleep are mainly represented in the first post-delivery phase. RLS and PLMS are frequent, with the first peak in the third trimester. Sleep macrostructure and the sleep-related breathing pattern appear to be only mildly affected by pregnancy

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Table 1: Assessment tools and time schedule of their administration of the 3 visits during pregnancy and the 6 visits during the post-partum period. All visits were performed face to face, except V5 and V7 (T), that were performed either in person or over the telephone depending on patient availability.

	PREGNANCY				**POSTPARTUM**					
	V0	**V1**	**V2**	**V3[(1)]**	**V4**	**V5 (T)**	**V6**	**V7 (T)**	**V8**	**V9**
	(10-15 W)	(10-15 W)	(23-25 W)	(34-36 W)	(1 W) (5-12 d)	(3 W) (19-26 d)	(5 W) (33-40 d)	(7 W) (47-54 d)	(3 M) (90-105 d)	(6 M) (180-195 d)
PSQI		•	•	•		•			•	•
ISI		•	•	•		•		•	•	•
ESS		•	•	•		•			•	•
RLS criteria + Severity Scale		•	•	•	•		•		•	•
MEQ		•								
PSG			•							

Table 2: The demographic and behavioral characteristics collected from the study group, with their summary statistics.

Categorical Variables	Categories	Number of observations	Relative percentage (%)
Marital status	**Total**	**439**	
	Married	257	58.5
	Cohabitation	178	40.5
	Single	3	0.7
	Divorced	1	0.2
Work	**Total**	**414**	
	Permanent position	280	67.6
	Fixed-term position	72	17.4
	Unemployed	62	15.0
Education	**Total**	**437**	
	Higher education	284	65.0
	Secondary education	129	29.5
	Primary education or less	24	5.5
Smoke	**Total**	**431**	
	No	403	93.5
	Yes	28	6.5
Alcohol	**Total**	**437**	

		No	420	96.1	
		Yes	17	3.9	
First Pregnancy		**Total**	**436**		
		No	247	56.7	
		Yes	189	43.3	
Twin pregnancy		**Total**	**439**		
		No	437	99.5	
		Yes	2	0.5	
Continuous variables		**Number of observations**	**Mean**	**Standard deviation**	
Age		439	33.720	4.210	
Number of cigarettes		28	5.462	3.772	
BMI		**Number of observations**	**Mean**	**Standard deviation**	**Percentage with BMI > 25**
	Visit 1	414	22.936	3.449	23.4
	Visit 2	353	24.713	3.447	38.0
	Visit 3	311	26.4	3.534	58.8
	Visit 4	135	24.589	3.544	38.5
	Visit 6	248	23.726	3.394	30.2
	Visit 8	193	23.711	3.482	31.1
	Visit 9	149	23.269	3.447	28.2

Table 3: Summary statistics of the polysomnographic data obtained from 353 women between the 23rd and 25th week of pregnancy. TRT = total recording time; TST = total sleep time; AHI = apnea hypopnea index; RDI = respiratory disturbance index; ODI = oxygen desaturation index; PLMSI = periodic limb movements index; AI = arousal index; SE = sleep efficiency; WASO = wake after sleep onset.

PSG parameters (unit)	Mean	Std. Dev.
TRT (min)	478.7	58.3
TST (min)	397.3	66.8
SE (%)	83.0	10.6
N1 (%)	11.1	4.1
N2 (%)	46.3	6.6
N3 (%)	22.3	6.8
REM (%)	20.2	4.2
Latency to N1 (min)	16.8	18.4
Latency to N2 (min)	19.5	19.3
Latency to REM (min)	83.6	40.6
AHI	1.4	1.9
AHI (supine)	2.2	3.7
AHI (non-supine)	0.9	1.5
AHI (REM)	5.2	6.9
ODI (3%)	0.8	1.8
Mean SaO2 (%)	94.5	11.6
PLMSI	10.5	17.3
AI	12.2	4.3
N. Awakenings	24.0	8.9
WASO (min)	65.5	45.9

Legend to the figures

Figure 1. Sleep scores over time, and the fraction of positive RLS (*bottom right*). The trends of the averaged ESS (*top left*), ISI (*top right*) and PSQI (*bottom left*) scores are shown, with standard deviations of the data indicated in light grey and bootstrap 95%-confidence intervals for the mean in dark grey. The horizontal red line marks the pathological threshold value used; the vertical red line indicates the time of delivery. The bars below the three figures with the ESS, ISI and PSQI scores indicate the percentage of women presenting with scores above the pathological threshold value.

Figure 2. A scatterplot of the RDI score of respiratory disturbance versus BMI, with the least-squares regression line.

Supplementary Material

eFigure 1. The Spearman rank correlation coefficient of the ESS and PSQI (*left*) and of the ESS and ISI scores (*right*) respectively, at visits 1, 2, 3, 5, 8 and 9, with the *p*-value of the significance test.

eFigure 2. The mean ESS, ISI and PSQI scores for primiparous and pluriparous women respectively with bootstrap 95% confidence intervals represented by the shaded areas. The threshold values used are indicated by thick horizontal lines; the vertical lines indicate the time of delivery. The *p*-values of a *t*-test for difference between means of the two groups of women are shown; bold *p*-values indicate significance at 0.05. No correction for multiple comparisons was performed.

eFigure 3. The mean ESS, ISI and PSQI scores for women of different ages, with the Spearman rank correlation coefficient between age and sleep quality per visit.

eFigure 4. The Spearman rank correlation coefficient of the PSQI score and age, at visits 1, 2, 3, 5, 8 and 9, with the *p*-value of the significance test.

eFigure 5. The Spearman rank correlation coefficient of the ISI and PSQI scores, at visits 1, 2, 3, 5, 8 and 9, with the *p*-values of the significance test indicated.

eFigure 6. The Spearman rank correlation coefficient of the ISI score and age, at visits 1, 2, 3, 5, 8 and 9, with the *p*-values of the significance test indicated.

eFigure 7. The Spearman rank correlation coefficient of the ESS score and age, at visits 1, 2, 3, 5, 8 and 9, with the *p*-value of the significance test.

eFigure 8. Percentages of the four phases of sleep, averaged over all centers of recruitment.

eFigure 9: Percentages of the four phases of sleep, per center of recruitment.