**Impact of Smoking on Sleep Macro– and Microstructure**

Minh Khoa TRUONG, MD; Mathieu BERGER, PhD; José HABA-RUBIO, MD; Francesca SICLARI, MD; Pedro MARQUES-VIDAL, MD, PhD\*; Raphaël HEINZER, MD, MPH\*

*\*These authors contributed equally.*

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# Supplemental methods

# Polysomnography procedure and sleep parameters

Participants were invited to attend the Centre for Investigation and Research in Sleep (CIRS) at the Lausanne University Hospital (CHUV, Lausanne, Switzerland). Participants were equipped with a polysomnography (PSG) recorder (Titanium, Embla Flaga, Reykjavik, Iceland) and underwent a full-night PSG at home. PSG setup specifications followed the 2007 American Academy Sleep Medicine (AASM) recommendations.1 Sleep was recorded on first night, and patients were instructed to go to bed on their usual schedule. Physiological parameters included EEG (central, occipital and frontal), electrooculogram (right and left eyes), surface electromyogram (chin and *anterior tibialis* muscle), electrocardiogram, thoracic and abdominal respiratory effort by respiratory inductance plethysmography, snoring and body position. In addition, oxygen saturation (SpO2) was recorded by pulse oximetry and airflow with a nasal cannula. Total recording time (TRT) was defined as time from beginning of recording to final awakening; total sleep time (TST) was defined as time from beginning of sleep (N1 stage) to final awakening, minus time spent awake after sleep onset; sleep efficiency was defined as the ratio of TST to time in bed; sleep onset latency was defined as the period between turning off the lights and beginning of sleep. Sleep stages are N1, N2, N3 and REM (rapid eye movement). Arousal index (ArI) was defined as the average number of arousals per hour of TST. Periodic limb movements in sleep index (PLMSI) was defined as the average number of PLMS per hour of TST. Apnoea-hypopnoea index (AHI) was the total number of apnoea and hypopnoea events divided by TST. Stage shifts are reported as total numbers per night. Oxygen desaturation index (ODI 3%) was defined as the average number of desaturation episodes ≥3% from baseline per hour. Time with oxygen saturation (SpO2) below 90% (T90) and mean SpO2 were also measured.

**Table S1.** Characteristics of included and excluded participants.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Included (n=3233)** | **Excluded (n=1831)** | **P-value** |
| Age (years) | 56.6 ± 10.2 | 59.8 ± 10.8 | <0.001 |
| Male, No. (%) | 1545 (47.8) | 812 (44.4) | 0.018 |
| BMI (kg/m2) | 25.9 ± 4.3 | 26.8 ± 5.1 | <0.001 |
| BMI categories, No. (%) |  |  | <0.001 |
| Normal | 1489 (46.1) | 691 (39.1) |  |
| Overweight | 1274 (39.4) | 686 (38.8) |  |
| Obese | 470 (14.5) | 389 (22.0) |  |
| Waist-to-hip ratio | 0.91 ± 0.07 | 0.93 ± 0.07 | <0.001 |
| Living alone, No. (%) | 1310 (40.5) | 892 (48.7) | <0.001 |
| Education level, No. (%) |  |  | <0.001 |
| University | 772 (23.9) | 307 (16.8) |  |
| High school | 883 (27.3) | 423 (23.2) |  |
| Apprenticeship | 1155 (35.7) | 641 (35.1) |  |
| Mandatory education | 423 (13.1) | 455 (24.9) |  |
| Sedentary behaviour, No. (%) | 1803 (55.8) | 602 (63.5) | <0.001 |
| Smoking status, No. (%) |  |  | 0.023 |
| Never | 1353 (41.9) | 682 (38.4) |  |
| Former | 1209 (37.4) | 674 (38.0) |  |
| Current | 671 (20.8) | 418 (23.6) |  |
| Alcohol intake (units/week) | 4 [1–9] | 3 [0–8] | <0.001\* |
| Caffeine intake, No. (%) |  |  | <0.001 |
| None | 209 (6.5) | 154 (8.9) |  |
| 1 to 3 units/day | 2115 (65.4) | 1175 (67.6) |  |
| 4 to 6 units/day | 795 (24.6) | 339 (19.5) |  |
| >6 units/day | 114 (3.5) | 70 (4.0) |  |
| Depression, No. (%) | 382 (11.8) | 219 (20.7) | <0.001 |
| Anxiety, No. (%) | 93 (3.6) | 35 (2.6) | 0.104 |
| Psychoactive medication, No. (%) | 163 (5.0) | 200 (10.9) | <0.001 |
| Total number of medications | 1.5 ± 2.0 | 2.3 ± 2.7 | <0.001 |
| High blood pressure, No. (%) | 1269 (39.3) | 827 (45.3) | <0.001 |

Abbreviations: BMI, body mass index.

Results expressed as number of participants (%) for categorical variables and mean ± standard deviation or median [interquartile range] for continuous variables. p-values from Pearson chi-square, student’s t-test or nonparametric Kruskal-Wallis test\*.

**Table S2.** Characteristics of participants with subjective sleep variables only, and with both subjective and objective sleep variables.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Subjective variables only (n=1744)** | **Subjective and objective variables (n=1489)** | **P-value** |
| Age (years) | 56.6 ± 10.1 | 56.7 ± 10.3 | 0.584 |
| Male, No. (%) | 799 (45.8) | 746 (50.1) | 0.015 |
| BMI (kg/m2) | 25.8 ± 4.5 | 25.9 ± 4.2 | 0.479 |
| BMI categories, No. (%) |  |  | 0.052 |
| Normal | 821 (47.1) | 668 (44.8) |  |
| Overweight | 655 (37.5) | 619 (41.6) |  |
| Obese | 268 (15.4) | 202 (13.6) |  |
| Waist-to-hip ratio | 0.91 ± 0.07 | 0.91 ± 0.07 | 0.685 |
| Living alone, No. (%) | 725 (41.6) | 585 (39.3) | 0.188 |
| Education level, No. (%) |  |  | 0.073 |
| University | 421 (24.2) | 351 (23.6) |  |
| High school | 454 (26.0) | 429 (28.8) |  |
| Apprenticeship | 619 (35.5) | 536 (36.0) |  |
| Mandatory education | 250 (14.3) | 173 (11.6) |  |
| Sedentary behaviour, No. (%) | 994 (57.0) | 809 (54.3) | 0.129 |
| Smoking status, No. (%) |  |  | 0.027 |
| Never | 726 (41.6) | 627 (42.1) |  |
| Former | 627 (36.0) | 582 (39.1) |  |
| Current | 391 (22.4) | 280 (18.8) |  |
| Alcohol intake (units/week) | 4 [1 - 9] | 4 [1 - 10] | 0.074 \* |
| Caffeine intake, No. (%) |  |  | 0.928 |
| None | 116 (6.7) | 93 (6.3) |  |
| 1 to 3 units/day | 1142 (65.5) | 973 (65.3) |  |
| 4 to 6 units/day | 423 (24.2) | 372 (25.0) |  |
| >6 units/day | 63 (3.6) | 51 (3.4) |  |
| Depression, No. (%) | 199 (11.4) | 183 (12.3) | 0.440 |
| Anxiety, No. (%) | 43 (3.4) | 50 (3.7) | 0.664 |
| Psychoactive medication, No. (%) | 83 (4.8) | 80 (5.4) | 0.427 |
| Total number of medications | 1.4 ± 1.9 | 1.5 ± 2.0 | 0.316 |
| High blood pressure, No. (%) | 678 (38.9) | 591 (39.7) | 0.624 |

Abbreviations: BMI, body mass index.

Results expressed as number of participants (%) for categorical variables and mean ± standard deviation or median [interquartile range] for continuous variables. p-values from Pearson chi-square, student’s t-test or nonparametric Kruskal-Wallis test\*.

**Table S3.** Bivariate associations between subjective sleep characteristics (n=3233), sleep macrostructure (n=1489) and smoking status.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Never** | **Former** | **Current** | **P-value** |
| **Subjective sleep (n)** | 1353 | 1209 | 671 |  |
| PSQI | 4.7 ± 3.1 | 4.7 ± 2.9 | 4.6 ± 3.1 | 0.830 |
| ESS | 5.6 ± 3.8 | 6.2 ± 3.7 | 6.3 ± 3.7 | <0.001 |
| RLS (%) | 156 (13.3) | 154 (14.7) | 91 (15.6) | 0.385 |
| **Sleep macrostructure (n)** | 627 | 582 | 280 |  |
| TST (min) | 406 ± 69 | 395 ± 67 | 398 ± 77 | 0.028 |
| TRT (min) | 495 ± 68 | 489 ± 70 | 477 ± 78 | 0.002 |
| Sleep efficiency (%) | 85.1 ± 10.7 | 83.8 ± 10.8 | 87.1 ± 10.4 | <0.001 |
| Sleep onset latency (min) | 16 ± 22 | 14 ± 16 | 19 ± 24 | 0.014 |
| N1 stage (% of TST) | 11.5 ± 6.5 | 12.3 ± 7.7 | 12 ± 7.3 | 0.158 |
| N2 stage (% of TST) | 46.3 ± 9.8 | 45.3 ± 10 | 45.4 ± 9.4 | 0.217 |
| N3 stage (% of TST) | 20.1 ± 8.3 | 20.4 ± 8.4 | 20.2 ± 8.3 | 0.833 |
| REM sleep (% of TST) | 22.2 ± 6.0 | 22.0 ± 6.1 | 22.5 ± 6.1 | 0.546 |
| ArI (N/h) | 21 ± 11 | 21 ± 11 | 20 ± 10 | 0.113 |
| PLMSI (N/h) | 1 [0–19] | 3 [0–19] | 1 [0–16] | 0.451\* |
| AHI (N/h) | 10 [4–20] | 11 [5–21] | 8 [3–18] | 0.033\* |
| Stage shifts (N/nights) | 141 ± 50 | 141 ± 47 | 137 ± 47 | 0.462 |
| ODI 3% (N/h) | 10 [4–18] | 10 [5–20] | 8 [3–17] | 0.021\* |
| T90 (min) | 0.1 [0–1.0] | 0.1 [0–2.1] | 0.2 [0–2.2] | 0.007\* |
| Mean SpO2 (%) | 94 ± 2 | 94 ± 2 | 93 ± 6 | <0.001 |

Abbreviations: AHI, apnoea-hypopnoea index (according to 2012 AASM criteria); ArI, arousal index; ESS, Epworth Sleepiness Scale; ODI 3%, oxygen desaturation index; PLMSI, periodic limb movements in sleep index; PSQI, Pittsburgh Sleep Quality Index; RLS, restless legs syndrome; T90, time spent with oxygen saturation below 90%; TRT, total recording time; TST, total sleep time.

Results expressed as number of participants (percentage) for categorical variables and as mean ± standard deviation or median [interquartile range] for continuous variables. Between-groups comparisons performed using chi-square for categorical variables and analysis of variance or Kruskal-Wallis test\* for continuous variables.

**Table S4.** Bivariate association between relative EEG spectral power in sleep and smoking status.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Never (n=612)** | **Former (n=561)** | **Current (n=274)** | **P-value** |
| **N1** |  |  |  |  |
| Delta | 40.0 ± 6.8 | 40.1 ± 6.6 | 37.6 ± 6.2 | <0.001 |
| Theta | 11.3 ± 4.3 | 11.2 ± 4.3 | 10.6 ± 4.4 | 0.076 |
| Alpha | 10.6 ± 4.7 | 10.6 ± 4.7 | 10.5 ± 4.7 | 0.991 |
| Sigma | 4.7 ± 2.1 | 4.7 ± 2.0 | 4.8 ± 1.9 | 0.638 |
| Beta | 3.8 ± 2.5 | 3.9 ± 2.3 | 4.1 ± 3.0 | 0.244 |
| **N2** |  |  |  |  |
| Delta | 46.8 ± 5.9 | 47.1 ± 6.1 | 44.0 ± 6.1 | <0.001 |
| Theta | 8.7 ± 2.8 | 8.7 ± 2.9 | 8.5 ± 3.1 | 0.721 |
| Alpha | 7.6 ± 3.3 | 7.8 ± 3.4 | 8.4 ± 3.8 | 0.002 |
| Sigma | 4.4 ± 2.4 | 4.4 ± 2.3 | 5.0 ± 2.6 | 0.001 |
| Beta | 1.6 ± 1.1 | 1.6 ± 1.2 | 1.7 ± 1.1 | 0.230 |
| **N3** |  |  |  |  |
| Delta | 49.3 ± 6.0 | 49.9 ± 5.9 | 47.6 ± 6.7 | <0.001 |
| Theta | 4.9 ± 1.7 | 5.0 ± 1.6 | 4.7 ± 1.7 | 0.134 |
| Alpha | 3.5 ± 2.1 | 3.7 ± 2.0 | 4.2 ± 2.7 | <0.001 |
| Sigma | 1.5 ± 1.0 | 1.5 ± 0.9 | 1.7 ± 1.1 | 0.074 |
| Beta | 0.5 ± 0.5 | 0.5 ± 0.2 | 0.5 ± 0.5 | 0.610 |
| **N2N3** |  |  |  |  |
| Delta | 47.8 ± 5.8 | 48.2 ± 5.8 | 45.5 ± 6.3 | <0.001 |
| Theta | 6.8 ± 2.2 | 6.8 ± 2.3 | 6.5 ± 2.4 | 0.230 |
| Alpha | 5.6 ± 2.8 | 5.8 ± 2.8 | 6.3 ± 3.1 | 0.007 |
| Sigma | 3.1 ± 2.0 | 3.0 ± 1.8 | 3.3 ± 2.0 | 0.056 |
| Beta | 1.1 ± 1.0 | 1.1 ± 0.9 | 1.1 ± 1.0 | 0.607 |

EEG power reported as relative values (with respect to total power). Frequency bands: Delta (1–4 Hz), Theta (4–8 Hz), Alpha (8–12 Hz), Sigma (12-16 Hz), Beta (18-30 Hz).

Results expressed as mean ± standard deviation. Between-group comparisons performed using analysis of variance.

**Table S5.** Multivariable association between relative EEG spectral power in sleep and smoking status.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Never (n=612)** | **Former (n=561)** | **Current (n=274)** | **P-value** |
| **N1** |  |  |  |  |
| Delta | 40.1 ± 0.3 | 40.1 ± 0.3 | 37.5 ± 0.4a,b | <0.001 |
| Theta | 11.2 ± 0.2 | 11.1 ± 0.2 | 10.9 ± 0.2 | 0.622 |
| Alpha | 10.5 ± 0.2 | 10.6 ± 0.2 | 10.9 ± 0.3 | 0.514 |
| Sigma | 4.6 ± 0.1 | 4.6 ± 0.1 | 4.9 ± 0.1 | 0.196 |
| Beta | 3.8 ± 0.1 | 3.9 ± 0.1 | 4.1 ± 0.2 | 0.266 |
| **N2** |  |  |  |  |
| Delta | 46.9 ± 0.2 | 47.0 ± 0.3 | 44.2 ± 0.4a,b | <0.001 |
| Theta | 8.6 ± 0.1 | 8.6 ± 0.1 | 8.6 ± 0.2 | 0.985 |
| Alpha | 7.5 ± 0.1 | 7.8 ± 0.1 | 8.5 ± 0.2a | <0.001 |
| Sigma | 4.4 ± 0.1 | 4.4 ± 0.1 | 4.9 ± 0.2 | 0.007 |
| Beta | 1.6 ± 0.1 | 1.6 ± 0.1 | 1.7 ± 0.1 | 0.322 |
| **N3** |  |  |  |  |
| Delta | 49.2 ± 0.3 | 49.8 ± 0.3 | 48.0 ± 0.4b | <0.001 |
| Theta | 4.8 ± 0.1 | 4.9 ± 0.1 | 4.8 ± 0.1 | 0.453 |
| Alpha | 3.5 ± 0.1 | 3.8 ± 0.1 | 4.2 ± 0.1a | <0.001 |
| Sigma | 1.5 ± 0.1 | 1.5 ± 0.1 | 1.6 ±0.1 | 0.108 |
| Beta | 0.5 ± 0.1 | 0.4 ± 0.1 | 0.5 ±0.1 | 0.257 |
| **N2N3** |  |  |  |  |
| Delta | 47.8 ± 0.2 | 48.2 ± 0.2 | 45.8 ± 0.4a,b | <0.001 |
| Theta | 6.7 ± 0.1 | 6.8 ± 0.1 | 6.7 ±0.1 | 0.976 |
| Alpha | 5.6 ± 0.1 | 5.8 ± 0.1 | 6.4 ± 0.2a | <0.001 |
| Sigma | 3.0 ± 0.1 | 3.0 ± 0.1 | 3.3 ± 0.1 | 0.046 |
| Beta | 1.1 ± 0.1 | 1.0 ± 0.1 | 1.1 ± 0.1 | 0.273 |

EEG power reported as relative values (with respect to total power). Results expressed as multivariable-adjusted mean ± standard error. Frequency bands: Delta (1–4 Hz), Theta (4–8 Hz), Alpha (8–12 Hz), Sigma (12-16 Hz), Beta (18-30 Hz).

Between-group comparisons performed using analysis of variance adjusting for sex, age (continuous), body mass index categories (normal/overweight/obese), alcohol intake (continuous), marital status (alone/in couple), educational level (university/high school/apprenticeship/mandatory), sedentary status (yes/no), caffeine intake (none/1-3/4-6/>6), depression (yes/no), psychoactive medication (yes/no), total number of medications (continuous), high blood pressure (yes/no), and mean nocturnal SpO2 (continuous). Post-hoc comparisons conducted using Scheffe’s method. Results differing at p<0.005: a significantly different vs. never smokers, b significantly different vs. formersmokers.

**Table S6.** Regression slopes between absolute EEG delta power in sleep and cigarette equivalents.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Unadjusted** | **P-value** | **Sex- and age-adjusted** | **P-value** |
| **N1** |  |  |  |  |
| Linear | 0.21 (–0.17; 0.58) | 0.278 | 0.25 (–0.13; 0.62) | 0.199 |
| Robust | –0.20 (–0.39; 0.00) | 0.048 | –0.13 (–0.31; 0.06) | 0.179 |
| **N2** |  |  |  |  |
| Linear | –0.11 (–0.51; 0.30) | 0.602 | –0.02 (–0.43; 0.38) | 0.916 |
| Robust | –0.44 (–0.73; –0.15) | 0.003 | –0.32 (–0.6; –0.04) | 0.023 |
| **N3** |  |  |  |  |
| Linear | –0.05 (–1.14; 1.04) | 0.932 | 0.23 (–0.85; 1.30) | 0.680 |
| Robust | –1.16 (–1.89; –0.44) | 0.002 | –0.87 (–1.55; –0.19) | 0.013 |
| **N2N3** |  |  |  |  |
| Linear | –0.08 (–0.76; 0.59) | 0.807 | 0.05 (–0.61; 0.72) | 0.875 |
| Robust | –0.68 (–1.15; –0.22) | 0.004 | 0.05 (–0.61; 0.72) | 0.875 |
| **Non-REM** |  |  |  |  |
| Linear | –0.04 (–0.69; 0.60) | 0.896 | 0.09 (–0.54; 0.73) | 0.769 |
| Robust | –0.62 (–1.06; –0.17) | 0.007 | –0.46 (–0.87; –0.06) | 0.026 |

Results expressed as slope (95% confidence interval) per increase in 10 cigarette equivalents.

# References for supplemental material

1. Iber C A-IS, Chesson A, Quan SF. *The AASM manual for the scoring of sleep and associated events: rules terminology and technical specifications.* 1st ed. Westchester, IL: American Academy of Sleep Medicine; 2007.