

ONLINE SUPPLEMENT

Obstructive sleep apnoea and 5-year cognitive decline in the elderly

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SUPPLEMENTARY METHODS

Cognitive assessment

- Mini-Mental State Examination (MMSE) [1]. This test assessed global cognitive functioning. It includes subtests of orientation, registration and recall of words, attention and calculation, language, and constructional praxis. The score ranges from 0 (minimum) to 30 (maximum).
- Free and Cued Selective Reminding Test (FCSRT) [2]. This test evaluates episodic verbal memory. Participants were asked to learn 16 words in groups of four, with each corresponding cue provided verbally by the tester (e.g., "fish" is the cue for the word "herring"). Initially, participants were asked to recall the words immediately after reading them, four by four. Then, three recall trials separated from each other by a distractive task (mental calculation for 20 seconds) were successively performed. Finally, a delayed recall of the list was requested 20 minutes later, first a delayed free recall and then a delayed cued recall (only for words that were not recalled during the delayed free recall). In our analyses, we considered two measures: delayed free recall and delayed total recall (calculated as the delayed free recall + correct delayed cued recall). For these measures, scores ranged from 0 (minimum) to 16 (maximum).
- Verbal fluency tasks [3]. This test evaluates executive control and verbal ability. Participants were asked to verbally generate as many words beginning with the letter "P" as possible in a 2-minute period (phonemic verbal fluency). Then, participants were instructed to generate examples of animals in a 2-minute period (semantic verbal fluency). Proper names were scored as incorrect. The score represented the number of correct words.
- DO-40 naming test (French adaptation of the Boston naming test) [4]. This test evaluates confrontational word retrieval. Participants were asked to name 40 pictures. The score ranges from 0 (minimum) to 40 (maximum).
- Constructional praxis task from the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) neuropsychological test battery [5]. This task evaluates visuospatial and visuoconstructive abilities. The task involved the copying of four figures of increasing complexity (circle, diamond, overlapping rectangles, and Necker cube). The score ranges from 0 (minimum) to 11 points (maximum).
- Stroop test Victoria version [6]. This test evaluates processing speed and attentional control (executive function). Twenty-four stimuli were presented to participants in three different conditions. Participants were asked to name the color of the stimuli as quickly as possible. In condition 1 (dot condition), dots were presented. In condition 2 (neutral-word condition), neutral words were presented. In condition 3 (color-word condition), the words *blue*, *green*, *yellow*, and *red* were written in one of the three other colors (e.g., the word *green* was written in yellow ink). In conditions 2 and 3, participants had to inhibit the written word to correctly name the ink color. In our analyses, we considered the

time (seconds) required to complete each condition, so that a higher time corresponded to a lower performance.

Conditions 1 and 2 are generally considered a measure of processing speed, whereas condition 3 is considered a measure of executive function.

Polysomnography

During a visit at the Center for Investigation and Research in Sleep (Lausanne University Hospital, Switzerland), trained technicians equipped the subjects with the polysomnographic (PSG) recorder (Titanium, Embla® Flaga, Reykjavik, Iceland) between 5 and 8 PM. Sleep recordings took place in the participants' home environment and included a total of 18 channels, in accordance with 2007 American Academy of Sleep Medicine recommended setup specifications [7]: 6 electroencephalography, 2 electrooculography, 3 surface electromyography (1 submental, 2 for right and left anterior tibialis muscles), 1 for electrocardiogram, nasal pressure, thoracic and abdominal belts, body position, oxygen saturation, and pulse rate. All PSG recordings were visually scored by two trained sleep technicians using Somnologica software (Version 5.1.1, by Embla® Flaga, Reykjavik, Iceland) and reviewed by a trained sleep physician. Random quality checks were performed by a second sleep physician.

Genotyping

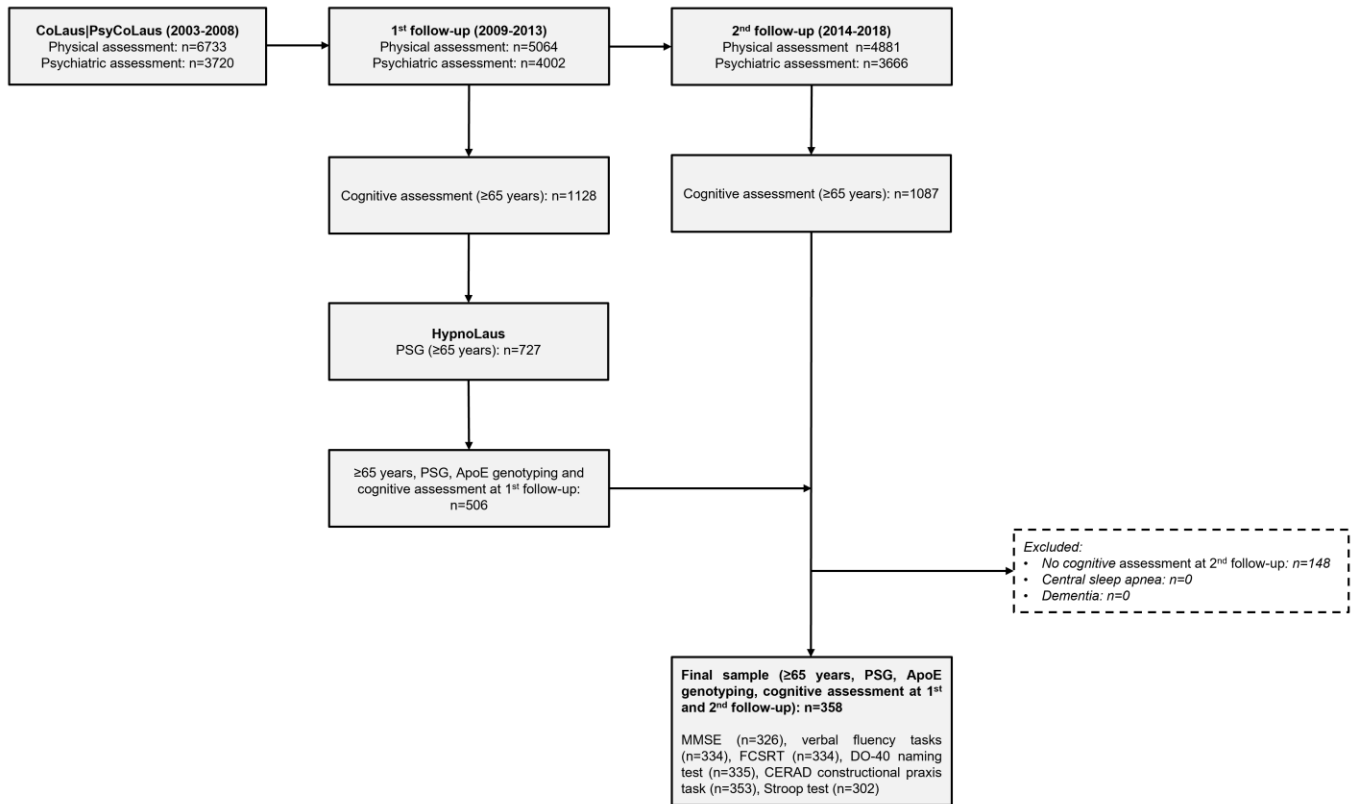
Genome-wide genotyping was performed using the Affymetrix 500K SNP array. Nuclear DNA was extracted from the whole blood of all participants. Genotypes were called using BRLMM (http://www.affymetrix.com/support/technical/whitepapers/brlmm_whitepap). Subjects were excluded from the analysis if there was inconsistency between sex and genetic data, a genotype call rate <90%, or inconsistencies of genotyping results in duplicate samples. Quality control for single nucleotide polymorphisms was performed using the following criteria: monomorphic (or with minor allele frequency <1%), call rates <90%, deviation from the Hardy-Weinberg equilibrium ($p < 1 \times 10^{-6}$). Phased haplotypes were generated using SHAPEIT2 [8], [9]. Imputation was performed using minimac3 [10] and the Haplotype Reference Consortium (HRC version r1.1) [11] hosted on the Michigan Imputation Server [10].

Handling of missing data

- Cognitive data: analysis restricted to records with available data (see **Figure 1** and **S1**).
- Hypoxic burden ($n = 18$): sensitivity analysis excluding participants without data.
- Body mass index ($n = 3$) and hypertension ($n = 1$): data recorded at the baseline of the CoLaus|PsyCoLaus study were used.

SUPPLEMENTARY FIGURES

Figure S1. Flowchart of the study population.



Abbreviations: ApoE = apolipoprotein E; CERAD = Consortium to Establish a Registry for Alzheimer's Disease; FCSRT = Free and Cued Selective Reminding Test; MMSE = Mini-Mental State Examination; PSG = polysomnography.

SUPPLEMENTARY TABLES

Table S1. Cognitive tests and corresponding significant decline.

| Cognitive test | Worsening corresponding to a significant decline at 5-year follow-up | Incidence of significant cognitive decline at follow-up, n (%) |
|--|--|--|
| MMSE (n=326) | ≥ 2.0 points | 45 (13.8) |
| Stroop test condition 1 (n=302) | ≥ 7.3 seconds | 22 (7.2) |
| Stroop test condition 2 (n=302) | ≥ 10.2 seconds | 27 (8.9) |
| Stroop test condition 3 (n=302) | ≥ 17.7 seconds | 26 (8.6) |
| Phonemic fluency (n=334) | ≥ 7.6 points | 51 (15.3) |
| Semantic fluency (n=334) | ≥ 9.3 points | 53 (15.9) |
| FCSRT delayed free recall (n=334) | ≥ 3.2 points | 58 (17.4) |
| FCSRT delayed total recall (n=334) | ≥ 1.8 points | 29 (8.8) |
| DO-40 naming test (n=335) | ≥ 1.9 points | 20 (6.0) |
| CERAD constructional praxis task (n=353) | ≥ 2.0 points | 34 (9.6) |

Abbreviations: CERAD = Consortium to Establish a Registry for Alzheimer's Disease; FCSRT = Free and Cued Selective Reminding Test; MMSE = Mini-Mental State Examination.

Table S2. Baseline characteristics of included participants and excluded individuals (excluded individuals had only a baseline cognitive assessment but no cognitive assessment at follow-up).

| | Included participants (n=358) | Excluded individuals (n=148) | Test | P |
|--|----------------------------------|---------------------------------|----------------|------------------|
| Clinical characteristics | | | | |
| Age, years | 71.0 ± 4.2 | 72.3 ± 4.8 | t = 0.7 | 0.388 |
| Men, n (%) | 152 (42.5) | 78 (52.7) | $\chi^2 = 3.6$ | 0.059 |
| ApoE4 carriers, n (%) | 83 (23.2) | 26 (17.6) | $\chi^2 = 3.7$ | 0.054 |
| Education (≥high school), n (%) | 150 (41.9) | 61 (41.2) | $\chi^2 = 0.1$ | 0.698 |
| BMI, kg/m ² | 26.8 ± 4.5 | 27.4 ± 4.6 | t = 0.3 | 0.553 |
| Diabetes, n (%) | 54 (15.1) | 35 (23.6) | $\chi^2 = 5.8$ | 0.016 |
| Hypertension, n (%) | 236 (65.9) | 97 (65.5) | $\chi^2 = 0.1$ | 0.762 |
| Smoking, n (%) | 199 (55.6) | 80 (54.0) | $\chi^2 = 0.1$ | 0.724 |
| Alcohol (≥14 units/week), n (%) | 65 (18.2) | 24 (16.2) | $\chi^2 = 0.1$ | 0.723 |
| Psychotropic drugs, n (%) | 67 (18.7) | 44 (29.7) | $\chi^2 = 7.7$ | 0.005 |
| Epworth Sleepiness Scale, points | 5.2 ± 3.4 | 4.9 ± 2.9 | t = 0.7 | 0.082 |
| Depression, n (%) | 138 (41.9) | 43 (29.0) | $\chi^2 = 4.7$ | 0.030 |
| CPAP, n (%) | 8 (2.2) | 2 (1.3) | Fisher | 0.590 |
| COPD, n (%) | 10 (2.8) | 8 (5.4) | Fisher | 0.062 |
| Sleep characteristics | | | | |
| AHI, events/h | 13.8 [0.0, 88.1] | 17.5 [0.1, 135.1] | U = 21610 | 0.010 |
| ODI, events/h | 13.5 [0.1, 84.4] | 17.4 [0.1, 121.3] | U = 21631 | 0.010 |
| Mean SpO ₂ , % | 93.4 ± 1.6 | 93.1 ± 1.9 | t = 1.8 | 0.072 |
| TST90, % | 0.8 [0.0, 91.9] | 2.3 [0.0, 100.0] | U = 21578 | 0.009 |
| Hypoxic burden, %min/h | 19.3 [0.1, 269.3] | 19.3 [0.1, 237.8] | U = 24170 | <0.001 |
| Sleep efficiency, % | 81.9 [29.6, 96.6] | 75.5 [32.5, 97.8] | U = 20196 | <0.001 |
| Arousal index, events/h | 22.7 [4.4, 104.6] | 26.6 [7.1, 73.9] | U = 24286 | 0.465 |
| Cognitive characteristics | | | | |
| MMSE, points | 30.0 [22.0, 30.0] | 30.0 [18.0, 30.0] | U = 19837 | 0.002 |
| Phonemic fluency, points | 21.6 ± 8.1 | 19.8 ± 7.5 | t = 2.1 | 0.035 |
| Semantic fluency, points | 31.0 ± 8.3 | 27.7 ± 7.8 | t = 3.9 | <0.001 |
| FCSRT delayed free recall, points | 11.9 ± 2.5 | 10.9 ± 3.0 | t = 3.3 | 0.001 |
| FCSRT delayed total recall, points | 16.0 [10.0, 16.0] | 16.0 [10.0, 16.0] | U = 19004 | 0.338 |
| DO-40 naming test, points | 40.0 [37.0, 40.0] | 40.0 [24.0, 40.0] | U = 21449 | 0.629 |
| CERAD constructional praxis task, points | 11.0 [5.0, 11.0] | 11.0 [4.0, 11.0] | U = 22084 | 0.005 |
| Stroop test condition 1, seconds | 16.4 ± 6.2 | 18.3 ± 6.5 | t = 3.1 | 0.002 |
| Stroop test condition 2, seconds | 20.9 ± 6.5 | 23.9 ± 8.7 | t = 4.2 | <0.001 |
| Stroop test condition 3, seconds | 32.8 ± 11.8 | 37.6 ± 13.8 | t = 3.9 | <0.001 |

Data are presented as mean ± standard deviation, median [range] or number of participants (%). Data were analysed using unpaired T-test (t), Mann-Whitney U test (U), chi-squared test (χ^2) or Fisher's exact test. Bold text indicates significant results (P < 0.05). Abbreviations: AHI = apnoea-hypopnoea index; ApoE4 = apolipoprotein E4; BMI = body mass index; CERAD = Consortium to Establish a Registry for Alzheimer's Disease; COPD = chronic obstructive pulmonary disease; CPAP = continuous positive airway pressure; FCSRT = Free and Cued Selective Reminding Test; MMSE = Mini-Mental State Examination; ODI = oxygen desaturation index; SpO₂ = oxygen saturation; TST90 = sleep time with oxygen saturation <90%.

Table S3. Associations between obstructive sleep apnoea parameters and annual change in cognitive scores.

| | Annual change in cognitive scores | | | | | |
|---------------------------|-----------------------------------|--------------|---------------|--------------|---------------|--------------|
| | Model 1 | | Model 2 | | Model 3 | |
| | <i>B</i> (SE) | P | <i>B</i> (SE) | P | <i>B</i> (SE) | P |
| MMSE | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | -0.02 (0.04) | 0.502 | -0.02 (0.04) | 0.583 | -0.02 (0.04) | 0.603 |
| <15 (n=184; ref.) | | | | | | |
| Cont. (10-unit increase) | -0.01 (0.01) | 0.528 | -0.00 (0.01) | 0.577 | -0.00 (0.01) | 0.601 |
| ODI (events/h) | | | | | | |
| ≥15 (n=172) | -0.03 (0.04) | 0.391 | -0.03 (0.04) | 0.490 | -0.03 (0.04) | 0.484 |
| <15 (n=186; ref.) | | | | | | |
| Cont. (10-unit increase) | -0.01 (0.01) | 0.331 | -0.01 (0.01) | 0.412 | -0.01 (0.01) | 0.450 |
| Mean SpO ₂ (%) | | | | | | |
| ≤92.5 (n=88) | -0.12 (0.04) | 0.003 | -0.12 (0.04) | 0.004 | -0.12 (0.04) | 0.004 |
| >92.5 (n=270; ref.) | | | | | | |
| Cont. (1-unit decrease) | -0.02 (0.01) | 0.024 | -0.03 (0.12) | 0.024 | -0.03 (0.01) | 0.023 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | -0.08 (0.04) | 0.056 | -0.07 (0.04) | 0.115 | -0.07 (0.04) | 0.111 |
| <4.5 (n=266; ref.) | | | | | | |
| Cont. (1-unit increase) | 0.00 (0.01) | 0.223 | 0.00 (0.01) | 0.328 | 0.00 (0.00) | 0.299 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | 0.01 (0.04) | 0.871 | 0.01 (0.04) | 0.789 | 0.01 (0.04) | 0.811 |
| >72 (n=271; ref.) | | | | | | |
| Cont. (10-unit decrease) | 0.01 (0.02) | 0.656 | 0.01 (0.02) | 0.474 | 0.01 (0.02) | 0.476 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | 0.03 (0.04) | 0.426 | 0.04 (0.04) | 0.376 | 0.04 (0.04) | 0.359 |
| <32 (n=268; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.01 (0.01) | 0.634 | 0.01 (0.01) | 0.647 | 0.01 (0.01) | 0.643 |
| Phonemic fluency | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | -0.16 (0.15) | 0.286 | -0.22 (0.15) | 0.147 | -0.23 (0.16) | 0.139 |
| <15 (n=184; ref.) | | | | | | |
| Cont. (10-unit increase) | -0.02 (0.04) | 0.545 | -0.04 (0.04) | 0.315 | -0.04 (0.04) | 0.313 |
| ODI (events/h) | | | | | | |
| ≥15 (n=172) | -0.20 (0.15) | 0.172 | -0.27 (0.16) | 0.087 | -0.27 (0.16) | 0.080 |
| <15 (n=186; ref.) | | | | | | |
| Cont. (10-unit increase) | -0.04 (0.05) | 0.400 | -0.06 (0.05) | 0.234 | -0.06 (0.05) | 0.235 |
| Mean SpO ₂ (%) | | | | | | |
| ≤92.5 (n=88) | -0.16 (0.17) | 0.330 | -0.18 (0.17) | 0.283 | -0.19 (0.17) | 0.268 |
| >92.5 (n=270; ref.) | | | | | | |
| Cont. (1-unit decrease) | -0.06 (0.04) | 0.193 | -0.07 (0.05) | 0.139 | -0.06 (0.05) | 0.170 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | -0.10 (0.17) | 0.557 | -0.07 (0.17) | 0.662 | -0.08 (0.17) | 0.635 |
| <4.5 (n=266; ref.) | | | | | | |
| Cont. (1-unit increase) | 0.00 (0.05) | 0.344 | 0.00 (0.00) | 0.408 | 0.00 (0.00) | 0.473 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | -0.20 (0.17) | 0.238 | -0.19 (0.17) | 0.254 | -0.20 (0.17) | 0.227 |
| >72 (n=271; ref.) | | | | | | |
| Cont. (10-unit decrease) | -0.07 (0.06) | 0.246 | 0.06 (0.06) | 0.355 | -0.06 (0.06) | 0.335 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | -0.06 (0.17) | 0.708 | -0.11 (0.17) | 0.535 | -0.09 (0.17) | 0.608 |
| <32 (n=268; ref.) | | | | | | |

| | | | | | | |
|-----------------------------------|--------------|-------|--------------|--------------|--------------|--------------|
| Cont. (10-unit increase) | -0.02 (0.06) | 0.762 | -0.05 (0.06) | 0.421 | -0.04 (0.06) | 0.485 |
| Semantic fluency | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | -0.02 (0.17) | 0.919 | -0.03 (0.18) | 0.847 | -0.02 (0.18) | 0.929 |
| <15 (n=184; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.00 (0.05) | .997 | 0.00 (0.05) | 0.963 | 0.00 (0.00) | 0.934 |
| ODI (events/h) | | | | | | |
| ≥15 (n=172) | 0.05 (0.17) | 0.768 | 0.06 (0.18) | 0.747 | 0.08 (0.18) | 0.676 |
| <15 (n=186; ref.) | | | | | | |
| Cont. (10-unit increase) | -0.01 (0.05) | 0.905 | -0.01 (0.06) | 0.889 | 0.00 (0.06) | 0.956 |
| Mean SpO ₂ (%) | | | | | | |
| ≤92.5 (n=88) | -0.29 (0.19) | 0.132 | -0.33 (0.19) | 0.097 | -0.31 (0.20) | 0.117 |
| >92.5 (n=270; ref.) | | | | | | |
| Cont. (1-unit decrease) | -0.05 (0.05) | 0.297 | -0.07 (0.05) | 0.204 | -0.06 (0.05) | 0.238 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | -0.07 (0.20) | 0.699 | -0.06 (0.20) | 0.767 | -0.04 (0.20) | 0.827 |
| <4.5 (n=266; ref.) | | | | | | |
| Cont. (1-unit increase) | 0.00 (0.01) | 0.946 | 0.00 (0.01) | 0.965 | 0.00 (0.06) | 0.998 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | 0.23 (0.19) | 0.241 | 0.21 (0.19) | 0.265 | 0.21 (0.19) | 0.272 |
| >72 (n=271; ref.) | | | | | | |
| Cont. (10-unit decrease) | 0.11 (0.07) | 0.134 | 0.11 (0.07) | 0.129 | 0.12 (0.07) | 0.109 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | -0.44 (0.19) | 0.024 | -0.47 (0.20) | 0.018 | -0.46 (0.20) | 0.020 |
| <32 (n=268; ref.) | | | | | | |
| Cont. (10-unit increase) | -0.01 (0.16) | 0.072 | -0.14 (0.07) | 0.039 | -0.13 (0.07) | 0.040 |
| FCSRT delayed free recall | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | -0.01 (0.06) | 0.930 | -0.03 (0.07) | 0.612 | -0.04 (0.07) | 0.572 |
| <15 (n=184; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.00 (0.02) | 0.788 | 0.00 (0.02) | 0.909 | 0.00 (0.02) | 0.883 |
| ODI (events/h) | | | | | | |
| ≥15 (n=172) | 0.04 (0.06) | 0.498 | 0.02 (0.07) | 0.798 | 0.02 (0.07) | 0.817 |
| <15 (n=186; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.00 (0.02) | 0.864 | -0.01 (0.02) | 0.494 | -0.01 (0.02) | 0.473 |
| Mean SpO ₂ (%) | | | | | | |
| ≤92.5 (n=88) | -0.12 (0.07) | 0.079 | -0.15 (0.07) | 0.034 | -0.16 (0.07) | 0.026 |
| >92.5 (n=270; ref.) | | | | | | |
| Cont. (1-unit decrease) | -0.04 (0.02) | 0.035 | -0.05 (0.02) | 0.006 | -0.05 (0.02) | 0.008 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | -0.09 (0.07) | 0.177 | -0.13 (0.07) | 0.071 | -0.13 (0.07) | 0.068 |
| <4.5 (n=266; ref.) | | | | | | |
| Cont. (1-unit increase) | 0.00 (0.00) | 0.048 | 0.00 (0.02) | 0.019 | 0.00 (0.00) | 0.024 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | 0.05 (0.07) | 0.501 | 0.04 (0.07) | 0.553 | 0.04 (0.07) | 0.595 |
| >72 (n=271; ref.) | | | | | | |
| Cont. (10-unit decrease) | 0.02 (0.03) | 0.460 | 0.02 (0.03) | 0.481 | 0.02 (0.03) | 0.494 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | 0.11 (0.07) | 0.125 | 0.09 (0.07) | 0.201 | 0.11 (0.07) | 0.148 |
| <32 (n=268; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.00 (0.02) | 0.943 | -0.01 (0.02) | 0.777 | 0.00 (0.02) | 0.875 |
| FCSRT delayed total recall | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | 0.00 (0.03) | 0.968 | 0.00 (0.04) | 0.999 | 0.00 (0.04) | 0.984 |

| | | | | | | |
|---|--------------|-------|--------------|-------|--------------|-------|
| <15 (n=184; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.00 (0.01) | 0.811 | 0.00 (0.01) | 0.766 | 0.00 (0.01) | 0.808 |
| ODI (events/h) | | | | | | |
| ≥15 (n=172) | 0.02 (0.03) | 0.640 | 0.02 (0.04) | 0.664 | 0.02 (0.04) | 0.588 |
| <15 (n=186; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.00 (0.01) | 0.609 | -0.01 (0.01) | 0.520 | -0.01 (0.01) | 0.609 |
| Mean SpO ₂ (%) | | | | | | |
| ≤92.5 (n=88) | -0.02 (0.04) | 0.655 | -0.02 (0.04) | 0.651 | -0.01 (0.04) | 0.704 |
| >92.5 (n=270; ref.) | | | | | | |
| Cont. (1-unit decrease) | 0.00 (0.01) | 0.894 | 0.00 (0.01) | 0.905 | 0.00 (0.01) | 0.911 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | 0.00 (0.04) | 0.935 | -0.01 (0.04) | 0.783 | -0.01 (0.04) | 0.880 |
| <4.5 (n=266; ref.) | | | | | | |
| Cont. (1-unit increase) | 0.00 (0.00) | 0.552 | 0.00 (0.00) | 0.570 | 0.00 (0.01) | 0.708 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | 0.03 (0.04) | 0.451 | 0.03 (0.04) | 0.409 | 0.03 (0.04) | 0.454 |
| >72 (n=271; ref.) | | | | | | |
| Cont. (10-unit decrease) | 0.01 (0.01) | 0.561 | -0.01 (0.01) | 0.548 | 0.01 (0.01) | 0.511 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | 0.00 (0.01) | 0.945 | 0.00 (0.04) | 0.947 | 0.00 (0.04) | 0.911 |
| <32 (n=268; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.00 (0.01) | 0.816 | 0.00 (0.01) | 0.744 | 0.00 (0.01) | 0.833 |
| DO-40 naming test | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | 0.00 (0.03) | 0.937 | -0.01 (0.03) | 0.732 | -0.01 (0.30) | 0.687 |
| <15 (n=184; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.01 (0.01) | 0.139 | 0.01 (0.01) | 0.188 | 0.01 (0.01) | 0.227 |
| ODI (events/h) | | | | | | |
| ≥15 (n=172) | 0.02 (0.03) | 0.485 | 0.01 (0.03) | 0.626 | 0.01 (0.03) | 0.735 |
| <15 (n=186; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.01 (0.01) | 0.109 | 0.01 (0.01) | 0.144 | 0.01 (0.01) | 0.210 |
| Mean SpO ₂ (%) | | | | | | |
| ≤92.5 (n=88) | -0.03 (0.03) | 0.350 | -0.04 (0.03) | 0.209 | -0.05 (0.03) | 0.148 |
| >92.5 (n=270; ref.) | | | | | | |
| Cont. (1-unit decrease) | 0.00 (0.01) | 0.965 | 0.00 (0.01) | 0.781 | 0.00 (0.01) | 0.605 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | -0.02 (0.03) | 0.494 | -0.03 (0.03) | 0.293 | -0.04 (0.03) | 0.220 |
| <4.5 (n=266; ref.) | | | | | | |
| Cont. (1-unit increase) | 0.00 (0.00) | 0.778 | 0.00 (0.00) | 0.932 | 0.00 (0.00) | 0.923 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | -0.02 (0.03) | 0.621 | -0.01 (0.03) | 0.721 | -0.01 (0.03) | 0.772 |
| >72 (n=271; ref.) | | | | | | |
| Cont. (10-unit decrease) | -0.01 (0.01) | 0.437 | -0.01 (0.01) | 0.476 | -0.01 (0.01) | 0.416 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | 0.01 (0.03) | 0.838 | 0.00 (0.03) | 0.871 | 0.00 (0.03) | 0.999 |
| <32 (n=268; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.01 (0.01) | 0.222 | 0.01 (0.01) | 0.259 | 0.01 (0.01) | 0.295 |
| CERAD constructional praxis task | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | 0.00 (0.03) | 0.992 | -0.01 (0.03) | 0.846 | -0.01 (0.03) | 0.804 |
| <15 (n=184; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.01 (0.01) | 0.268 | 0.01 (0.01) | 0.336 | 0.01 (0.01) | 0.359 |
| ODI (events/h) | | | | | | |

| | | | | | | |
|--------------------------------|--------------|--------------|--------------|--------------|--------------|--------------|
| ≥15 (n=172) | 0.01 (0.03) | 0.676 | 0.01 (0.03) | 0.776 | 0.01 (0.03) | 0.822 |
| <15 (n=186; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.01 (0.01) | 0.244 | 0.01 (0.01) | 0.307 | 0.01 (0.01) | 0.341 |
| Mean SpO ₂ (%) | | | | | | |
| ≤92.5 (n=88) | -0.01 (0.03) | 0.786 | -0.01 (0.03) | 0.711 | -0.01 (0.03) | 0.673 |
| >92.5 (n=270; ref.) | | | | | | |
| Cont. (1-unit decrease) | 0.01 (0.01) | 0.225 | 0.01 (0.01) | 0.267 | 0.01 (0.10) | 0.292 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | 0.02 (0.03) | 0.561 | 0.01 (0.04) | 0.676 | 0.02 (0.04) | 0.643 |
| <4.5 (n=266; ref.) | | | | | | |
| Cont. (1-unit increase) | 0.00 (0.00) | 0.749 | 0.00 (0.00) | 0.753 | 0.00 (0.00) | 0.762 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | 0.01 (0.03) | 0.847 | 0.00 (0.03) | 0.887 | 0.01 (0.03) | 0.874 |
| >72 (n=271; ref.) | | | | | | |
| Cont. (10-unit decrease) | 0.00 (0.01) | 0.676 | 0.00 (0.01) | 0.741 | 0.00 (0.01) | 0.466 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | 0.02 (0.03) | 0.612 | 0.01 (0.03) | 0.737 | 0.01 (0.03) | 0.765 |
| <32 (n=268; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.00 (0.01) | 0.819 | 0.00 (0.01) | 0.961 | 0.00 (0.01) | 0.992 |
| Stroop test condition 1 | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | 0.05 (0.15) | 0.715 | 0.08 (0.15) | 0.620 | 0.07 (0.15) | 0.625 |
| <15 (n=184; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.03 (0.04) | 0.468 | 0.04 (0.04) | 0.383 | 0.04 (0.04) | 0.337 |
| ODI (events/h) | | | | | | |
| ≥15 (n=172) | 0.05 (0.15) | 0.741 | 0.07 (0.16) | 0.667 | 0.09 (0.16) | 0.580 |
| <15 (n=186; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.04 (0.00) | 0.395 | 0.05 (0.05) | 0.295 | 0.06 (0.05) | 0.250 |
| Mean SpO ₂ (%) | | | | | | |
| ≤92.5 (n=88) | 0.45 (0.16) | 0.006 | 0.51 (0.17) | 0.002 | 0.53 (0.17) | 0.002 |
| >92.5 (n=270; ref.) | | | | | | |
| Cont. (1-unit decrease) | 0.05 (0.04) | 0.249 | 0.07 (0.04) | 0.133 | 0.08 (0.04) | 0.080 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | 0.37 (0.17) | 0.028 | 0.43 (0.17) | 0.013 | 0.47 (0.17) | 0.006 |
| <4.5 (n=266; ref.) | | | | | | |
| Cont. (1-unit increase) | 0.00 (0.00) | 0.992 | 0.00 (0.00) | 0.956 | 0.00 (0.00) | 0.888 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | -0.11 (0.17) | 0.543 | -0.09 (0.17) | 0.594 | -0.09 (0.17) | 0.591 |
| >72 (n=271; ref.) | | | | | | |
| Cont. (10-unit decrease) | 0.01 (0.07) | 0.817 | 0.02 (0.07) | 0.799 | 0.02 (0.07) | 0.760 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | 0.06 (0.17) | 0.746 | 0.09 (0.17) | 0.603 | 0.11 (0.17) | 0.509 |
| <32 (n=268; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.01 (0.06) | 0.819 | 0.03 (0.06) | 0.618 | 0.03 (0.06) | 0.541 |
| Stroop test condition 2 | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | 0.01 (0.18) | 0.942 | 0.06 (0.19) | 0.760 | 0.06 (0.19) | 0.748 |
| <15 (n=184; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.01 (0.05) | 0.788 | 0.00 (0.05) | 0.927 | 0.00 (0.05) | 0.997 |
| ODI (events/h) | | | | | | |
| ≥15 (n=172) | -0.11 (0.18) | 0.546 | -0.08 (0.19) | 0.692 | -0.06 (0.19) | 0.769 |
| <15 (n=186; ref.) | | | | | | |
| Cont. (10-unit increase) | -0.01 (0.05) | 0.871 | 0.00 (0.06) | 0.942 | 0.01 (0.06) | 0.843 |
| Mean SpO ₂ (%) | | | | | | |

| | | | | | | |
|--------------------------------|--------------|-------|--------------|-------|--------------|-------|
| ≤92.5 (n=88) | 0.34 (0.20) | 0.091 | 0.39 (0.21) | 0.058 | 0.42 (0.21) | 0.045 |
| >92.5 (n=270; ref.) | | | | | | |
| Cont. (1-unit decrease) | 0.01 (0.05) | 0.876 | 0.02 (0.05) | 0.682 | 0.03 (0.06) | 0.557 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | 0.17 (0.20) | 0.396 | 0.22 (0.21) | 0.312 | 0.25 (0.22) | 0.253 |
| <4.5 (n=266; ref.) | | | | | | |
| Cont. (1-unit increase) | 0.00 (0.01) | 0.397 | 0.00 (0.01) | 0.447 | 0.00 (0.01) | 0.528 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | -0.46 (0.21) | 0.030 | -0.45 (0.21) | 0.033 | -0.46 (0.21) | 0.031 |
| >72 (n=271; ref.) | | | | | | |
| Cont. (10-unit decrease) | -0.13 (0.08) | 0.129 | -0.01 (0.08) | 0.113 | -0.13 (0.08) | 0.116 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | -0.16 (0.21) | 0.447 | -0.13 (0.21) | 0.544 | -0.12 (0.21) | 0.590 |
| <32 (n=268; ref.) | | | | | | |
| Cont. (10-unit increase) | -0.02 (0.07) | 0.789 | 0.00 (0.07) | 0.970 | 0.00 (0.07) | 0.961 |
| Stroop test condition 3 | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | -0.66 (0.31) | 0.036 | -0.74 (0.33) | 0.025 | -0.73 (0.33) | 0.027 |
| <15 (n=184; ref.) | | | | | | |
| Cont. (10-unit increase) | -0.16 (0.09) | 0.074 | -0.19 (0.10) | 0.046 | -0.19 (0.10) | 0.045 |
| ODI (events/h) | | | | | | |
| ≥15 (n=172) | -0.48 (0.31) | 0.130 | -0.56 (0.34) | 0.097 | -0.55 (0.34) | 0.100 |
| <15 (n=186; ref.) | | | | | | |
| Cont. (10-unit increase) | -0.15 (0.10) | 0.120 | -0.18 (0.01) | 0.078 | -0.18 (0.10) | 0.079 |
| Mean SpO ₂ (%) | | | | | | |
| ≤92.5 (n=88) | 0.52 (0.35) | 0.142 | 0.55 (0.36) | 0.130 | 0.60 (0.37) | 0.106 |
| >92.5 (n=270; ref.) | | | | | | |
| Cont. (1-unit decrease) | -0.03 (0.09) | 0.707 | -0.04 (0.10) | 0.683 | -0.04 (0.10) | 0.700 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | 0.03 (0.36) | 0.936 | -0.03 (0.38) | 0.935 | -0.03 (0.38) | 0.936 |
| <4.5 (n=266; ref.) | | | | | | |
| Cont. (1-unit increase) | 0.00 (0.01) | 0.589 | -0.01 (0.01) | 0.509 | -0.01 (0.01) | 0.503 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | 0.14 (0.37) | 0.704 | 0.14 (0.37) | 0.704 | 0.13 (0.37) | 0.717 |
| >72 (n=271; ref.) | | | | | | |
| Cont. (10-unit decrease) | 0.10 (0.15) | 0.508 | 0.08 (0.15) | 0.588 | 0.08 (0.15) | 0.594 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | -0.36 (0.37) | 0.333 | -0.34 (0.37) | 0.361 | -0.35 (0.38) | 0.354 |
| <32 (n=268; ref.) | | | | | | |
| Cont. (10-unit increase) | -0.11 (0.12) | 0.379 | -0.10 (0.13) | 0.443 | -0.10 (0.13) | 0.435 |

Data are presented as unstandardized beta coefficient (*B*) and standard error (SE). Data were analyzed by multivariable linear regression models using annual change in cognitive scores as dependent variable and each obstructive sleep apnoea parameter as independent variable. Bold text indicates significant results ($P < 0.01$). Model 1 = adjusted for age (continuous), sex (male, female), education (≥high school, <high school) and apolipoprotein E4 (carriers, non-carriers). Model 2 = model 1 additionally adjusted for body mass index (continuous), diabetes (yes, no), hypertension (yes, no), smoking (former or current, never), alcohol consumption (≥14, <14 units/week) and psychotropic drugs (yes, no). Model 3 = model 2 additionally adjusted for depression (yes, no), Epworth Sleepiness Scale (continuous), continuous positive airway pressure (yes, no) and chronic obstructive pulmonary disease (yes, no). Abbreviations: AHI = apnoea-hypopnoea index; CERAD = Consortium to Establish a Registry for Alzheimer's Disease; Cont. = continuous; FCSRT = Free and Cued Selective Reminding Test; MMSE = Mini-Mental State Examination; ODI = oxygen desaturation index; ref. = reference group; SpO₂ = oxygen saturation; TST90 = sleep time with oxygen saturation <90%.

Table S4. Associations between obstructive sleep apnoea parameters and incidence of significant cognitive decline.

| | Incidence of significant cognitive decline | | | | | |
|---------------------------|--|--------------|-------------------|--------------|-------------------|--------------|
| | Model 1 | | Model 2 | | Model 3 | |
| | OR (95% CI) | P | OR (95% CI) | P | OR (95% CI) | P |
| MMSE | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | 0.76 (0.38, 1.50) | 0.410 | 0.72 (0.35, 1.51) | 0.383 | 0.71 (0.34, 1.49) | 0.372 |
| <15 (n=184; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 0.96 (0.80, 1.14) | 0.625 | 0.96 (0.78, 1.16) | 0.661 | 0.95 (0.78, 1.16) | 0.654 |
| ODI (events/h) | | | | | | |
| ≥15 (n=172) | 0.78 (0.40, 1.52) | 0.452 | 0.75 (0.36, 1.55) | 0.431 | 0.76 (0.36, 1.57) | 0.456 |
| <15 (n=186; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 0.99 (0.82, 1.18) | 0.903 | 0.99 (0.80, 1.21) | 0.915 | 0.99 (0.80, 1.22) | 0.921 |
| Mean SpO ₂ (%) | | | | | | |
| ≤92.5 (n=88) | 2.88 (1.48, 5.59) | 0.002 | 3.23 (1.58, 6.61) | 0.001 | 3.27 (1.60, 6.72) | 0.001 |
| >92.5 (n=270; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit decrease) | 1.17 (1.01, 1.31) | 0.043 | 1.20 (1.02, 1.35) | 0.028 | 1.20 (1.01, 1.35) | 0.034 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | 2.01 (1.01, 4.00) | 0.047 | 2.04 (0.98, 4.27) | 0.057 | 2.02 (0.95, 4.27) | 0.066 |
| <4.5 (n=266; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit increase) | 1.01 (1.00, 1.03) | 0.113 | 1.01 (1.00, 1.03) | 0.118 | 1.01 (0.99, 1.03) | 0.164 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | 1.78 (0.89, 3.58) | 0.103 | 1.79 (0.88, 3.64) | 0.109 | 1.79 (0.88, 3.64) | 0.110 |
| >72 (n=271; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit decrease) | 1.09 (0.82, 1.41) | 0.532 | 1.06 (0.80, 1.38) | 0.659 | 1.04 (0.80, 1.34) | 0.675 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | 0.50 (0.22, 1.17) | 0.111 | 0.49 (0.21, 1.17) | 0.111 | 0.49 (0.20, 1.15) | 0.100 |
| <32 (n=268; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 0.82 (0.62, 1.07) | 0.147 | 0.82 (0.62, 1.08) | 0.166 | 0.81 (0.61, 1.07) | 0.149 |
| Phonemic fluency | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | 1.26 (0.67, 2.39) | 0.473 | 1.40 (0.70, 2.80) | 0.303 | 1.43 (0.71, 2.85) | 0.285 |
| <15 (n=184; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.03 (0.87, 1.19) | 0.154 | 1.05 (0.89, 1.24) | 0.066 | 1.21 (0.99, 1.47) | 0.070 |
| ODI (events/h) | | | | | | |
| ≥15 (n=172) | 1.39 (0.73, 2.64) | 0.291 | 1.62 (0.81, 3.27) | 0.166 | 1.66 (0.82, 3.37) | 0.147 |
| <15 (n=186; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.03 (0.88, 1.22) | 0.158 | 1.07 (0.89, 1.28) | 0.069 | 1.22 (0.99, 1.51) | 0.072 |
| Mean SpO ₂ (%) | | | | | | |
| ≤92.5 (n=88) | 0.93 (0.45, 1.92) | 0.852 | 0.97 (0.45, 2.08) | 0.947 | 0.98 (0.46, 2.11) | 0.971 |
| >92.5 (n=270; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit decrease) | 0.99 (0.78, 1.16) | 0.920 | 1.05 (0.86, 1.22) | 0.955 | 0.99 (0.76, 1.18) | 0.940 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | 0.90 (0.43, 1.90) | 0.798 | 0.90 (0.41, 1.96) | 0.787 | 0.90 (0.41, 1.99) | 0.801 |
| <4.5 (n=266; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit increase) | 0.99 (0.96, 1.02) | 0.884 | 0.99 (0.97, 1.01) | 0.887 | 1.00 (0.98, 1.02) | 0.820 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | 2.11 (1.07, 4.15) | 0.030 | 2.14 (1.08, 4.24) | 0.029 | 2.18 (1.09, 4.34) | 0.027 |
| >72 (n=271; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit decrease) | 1.34 (1.05, 1.71) | 0.021 | 1.33 (1.03, 1.71) | 0.027 | 1.34 (1.04, 1.72) | 0.026 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | 0.91 (0.42, 1.94) | 0.806 | 0.97 (0.44, 2.13) | 0.946 | 0.92 (0.42, 2.05) | 0.850 |
| <32 (n=268; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |

| | | | | | | |
|-----------------------------------|-------------------|--------------|-------------------|-------|--------------------|-------|
| Cont. (10-unit increase) | 1.06 (0.83, 1.34) | 0.633 | 0.99 (0.78, 1.27) | 0.415 | 1.09 (0.85, 1.41) | 0.484 |
| Semantic fluency | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | 0.91 (0.49, 1.71) | 0.778 | 0.88 (0.45, 1.73) | 0.808 | 0.87 (0.43, 1.69) | 0.750 |
| <15 (n=184; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.09 (0.93, 1.29) | 0.274 | 1.13 (0.93, 1.34) | 0.993 | 1.12 (0.93, 1.34) | 0.255 |
| ODI (events/h) | | | | | | |
| ≥15 (n=172) | 0.83 (0.44, 1.57) | 0.628 | 0.84 (0.43, 1.67) | 0.668 | 0.84 (0.42, 1.66) | 0.656 |
| <15 (n=186; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.10 (0.92, 1.33) | 0.283 | 1.15 (0.93, 1.40) | 0.211 | 1.14 (0.93, 1.40) | 0.238 |
| Mean SpO ₂ (%) | | | | | | |
| ≤92.5 (n=88) | 1.23 (0.62, 2.44) | 0.535 | 1.32 (0.65, 2.68) | 0.446 | 1.30 (0.64, 2.66) | 0.469 |
| >92.5 (n=270; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit decrease) | 1.04 (0.85, 1.20) | 0.677 | 1.06 (0.86, 1.23) | 0.564 | 1.06 (0.85, 1.23) | 0.603 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | 0.79 (0.38, 1.65) | 0.531 | 0.81 (0.38, 1.76) | 0.587 | 0.82 (0.38, 1.77) | 0.600 |
| <4.5 (n=266; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit increase) | 1.00 (0.97, 1.01) | 0.727 | 1.00 (0.98, 1.02) | 0.858 | 1.00 (0.97, 1.02) | 0.845 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | 1.00 (0.50, 2.03) | 0.991 | 1.02 (0.50, 2.07) | 0.954 | 1.03 (0.51, 2.10) | 0.931 |
| >72 (n=271; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit decrease) | 1.01 (0.77, 1.32) | 0.917 | 1.02 (0.78, 1.32) | 0.877 | 1.03 (0.82, 1.33) | 0.855 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | 2.08 (1.08, 4.02) | 0.029 | 2.16 (1.10, 4.26) | 0.026 | 2.14 (1.08, 4.24) | 0.029 |
| <32 (n=268; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.27 (1.06, 1.47) | 0.014 | 1.02 (1.07, 1.55) | 0.011 | 1.30 (1.072, 1.56) | 0.013 |
| FCSRT delayed free recall | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | 1.15 (0.70, 2.41) | 0.641 | 1.23 (0.63, 2.40) | 0.756 | 1.28 (0.65, 2.51) | 0.681 |
| <15 (n=184; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.07 (0.90, 1.25) | 0.435 | 1.05 (0.88, 1.24) | 0.564 | 1.05 (0.87, 1.25) | 0.552 |
| ODI (events/h) | | | | | | |
| ≥15 (n=172) | 1.06 (0.61, 2.08) | 0.841 | 0.97 (0.50, 1.84) | 0.927 | 1.08 (0.55, 2.10) | 0.930 |
| <15 (n=186; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.10 (0.93, 1.32) | 0.249 | 1.08 (0.89, 1.32) | 0.339 | 1.09 (0.89, 1.33) | 0.310 |
| Mean SpO ₂ (%) | | | | | | |
| ≤92.5 (n=88) | 2.30 (1.22, 4.34) | 0.015 | 2.09 (1.11, 4.33) | 0.031 | 2.33 (1.17, 4.66) | 0.021 |
| >92.5 (n=270; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit decrease) | 1.21 (1.07, 1.34) | 0.007 | 1.22 (1.05, 1.35) | 0.010 | 1.22 (1.05, 1.35) | 0.011 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | 1.83 (0.96, 3.48) | 0.083 | 1.75 (0.87, 3.52) | 0.117 | 1.90 (0.93, 3.84) | 0.082 |
| <4.5 (n=266; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit increase) | 1.02 (1.00, 1.04) | 0.012 | 1.02 (1.00, 1.03) | 0.030 | 1.01 (1.00, 1.03) | 0.036 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | 0.79 (0.38, 1.63) | 0.527 | 0.83 (0.40, 1.72) | 0.620 | 0.86 (0.41, 1.81) | 0.700 |
| >72 (n=271; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit decrease) | 0.92 (0.69, 1.22) | 0.586 | 0.93 (0.69, 1.24) | 0.647 | 0.95 (0.70, 1.27) | 0.725 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | 1.00 (0.49, 2.01) | 0.995 | 1.04 (0.50, 2.16) | 0.910 | 0.97 (0.46, 2.05) | 0.950 |
| <32 (n=268; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.08 (0.87, 1.34) | 0.481 | 1.09 (0.86, 1.37) | 0.438 | 1.06 (0.84, 1.34) | 0.560 |
| FCSRT delayed total recall | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | 1.43 (0.61, 3.32) | 0.404 | 1.49 (0.61, 3.66) | 0.379 | 1.52 (0.62, 3.75) | 0.350 |

| | | | | | | |
|---|-------------------|-------|-------------------|-------|-------------------|-------|
| <15 (n=184; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.05 (0.85, 1.28) | 0.665 | 1.04 (0.84, 1.29) | 0.710 | 1.05 (0.83, 1.32) | 0.698 |
| ODI (events/h) | | | | | | |
| ≥15 (n=172) | 1.20 (0.52, 2.74) | 0.665 | 1.17 (0.49, 2.84) | 0.713 | 1.14 (0.47, 2.80) | 0.755 |
| <15 (n=186; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.06 (0.85, 1.32) | 0.628 | 1.06 (0.83, 1.34) | 0.652 | 1.06 (0.82, 1.39) | 0.675 |
| Mean SpO ₂ (%) | | | | | | |
| ≤92.5 (n=88) | 1.40 (0.59, 3.33) | 0.436 | 1.27 (0.59, 3.23) | 0.606 | 1.32 (0.52, 3.35) | 0.554 |
| >92.5 (n=270; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit decrease) | 1.13 (0.90, 1.31) | 0.245 | 1.12 (0.87, 1.32) | 0.307 | 1.11 (0.85, 1.32) | 0.360 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | 0.97 (0.40, 2.37) | 0.951 | 0.92 (0.36, 2.37) | 0.855 | 0.93 (0.35, 2.45) | 0.875 |
| <4.5 (n=266; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit increase) | 1.02 (1.00, 1.04) | 0.105 | 1.02 (0.99, 1.04) | 0.136 | 1.01 (0.99, 1.04) | 0.209 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | 0.64 (0.24, 1.69) | 0.368 | 0.65 (0.24, 1.75) | 0.400 | 0.69 (0.25, 1.86) | 0.459 |
| >72 (n=271; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit decrease) | 0.86 (0.57, 1.25) | 0.440 | 0.86 (0.57, 1.25) | 0.447 | 0.85 (0.56, 1.27) | 0.439 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | 1.11 (0.45, 2.72) | 0.816 | 1.20 (0.47, 3.04) | 0.705 | 1.10 (0.43, 2.82) | 0.846 |
| <32 (n=268; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.13 (0.85, 1.48) | 0.410 | 1.15 (0.85, 1.54) | 0.373 | 1.13 (0.83, 1.52) | 0.448 |
| DO-40 naming test | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | 0.92 (0.31, 2.15) | 0.858 | 1.00 (0.36, 2.76) | 0.995 | 1.00 (0.36, 2.76) | 0.994 |
| <15 (n=184; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 0.81 (0.59, 1.12) | 0.191 | 0.81 (0.57, 1.14) | 0.218 | 0.81 (0.57, 1.14) | 0.220 |
| ODI (events/h) | | | | | | |
| ≥15 (n=172) | 0.73 (0.28, 1.90) | 0.524 | 0.79 (0.25, 2.21) | 0.655 | 0.80 (0.25, 2.07) | 0.671 |
| <15 (n=186; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 0.82 (0.95, 1.01) | 0.238 | 0.82 (0.57, 1.02) | 0.282 | 0.82 (0.58, 1.19) | 0.297 |
| Mean SpO ₂ (%) | | | | | | |
| ≤92.5 (n=88) | 2.01 (0.78, 5.18) | 0.127 | 2.59 (0.94, 7.11) | 0.065 | 3.01 (1.04, 8.70) | 0.035 |
| >92.5 (n=270; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit decrease) | 1.03 (0.71, 1.27) | 0.837 | 1.07 (0.73, 1.32) | 0.636 | 1.11 (0.76, 1.35) | 0.509 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | 1.78 (0.69, 4.60) | 0.243 | 2.30 (0.82, 6.70) | 0.112 | 2.50 (0.86, 7.25) | 0.102 |
| <4.5 (n=266; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit increase) | 1.01 (0.98, 1.04) | 0.481 | 1.02 (0.99, 1.04) | 0.302 | 1.02 (0.92, 1.05) | 0.213 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | 1.23 (0.45, 3.41) | 0.686 | 1.16 (0.41, 3.27) | 0.781 | 1.06 (0.37, 3.07) | 0.909 |
| >72 (n=271; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit decrease) | 1.07 (0.70, 1.58) | 0.750 | 1.05 (0.66, 1.55) | 0.826 | 1.02 (0.66, 1.54) | 0.920 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | 0.83 (0.28, 2.48) | 0.739 | 0.84 (0.27, 2.60) | 0.760 | 0.90 (0.28, 2.87) | 0.859 |
| <32 (n=268; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 0.69 (0.43, 1.07) | 0.113 | 0.66 (0.41, 1.07) | 0.098 | 0.66 (0.41, 1.08) | 0.104 |
| CERAD constructional praxis task | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | 0.76 (0.42, 1.38) | 0.287 | 0.71 (0.38, 1.33) | 0.388 | 0.72 (0.39, 1.35) | 0.307 |
| <15 (n=184; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 0.93 (0.75, 1.16) | 0.170 | 0.93 (0.74, 1.18) | 0.168 | 0.99 (0.97, 1.00) | 0.153 |
| ODI (events/h) | | | | | | |

| | | | | | | |
|--------------------------------|-------------------|--------------|--------------------|--------------|--------------------|--------------|
| ≥15 (n=172) | 0.91 (0.51, 1.64) | 0.690 | 0.89 (0.49, 1.70) | 0.719 | 0.93 (0.50, 1.74) | 0.762 |
| <15 (n=186; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 0.93 (0.74, 1.17) | 0.213 | 0.93 (0.73, 1.21) | 0.207 | 0.91 (0.71, 1.17) | 0.206 |
| Mean SpO ₂ (%) | | | | | | |
| ≤92.5 (n=88) | 0.90 (0.47, 1.73) | 0.757 | 0.91 (0.47, 1.82) | 0.784 | 0.96 (0.48, 1.91) | 0.913 |
| >92.5 (n=270; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit decrease) | 0.79 (0.54, 1.00) | 0.048 | 0.79 (0.48, 0.99) | 0.037 | 0.76 (0.48, 0.99) | 0.043 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | 0.79 (0.41, 1.52) | 0.461 | 0.77 (0.39, 1.55) | 0.466 | 0.72 (0.35, 1.47) | 0.359 |
| <4.5 (n=266; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit increase) | 1.01 (0.99, 1.03) | 0.622 | 0.99 (0.98, 1.03) | 0.624 | 0.99 (0.97, 1.02) | 0.582 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | 1.09 (0.56, 2.09) | 0.804 | 1.08 (0.56, 2.09) | 0.813 | 1.06 (0.55, 2.07) | 0.860 |
| >72 (n=271; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit decrease) | 1.12 (0.84, 1.38) | 0.524 | 1.09 (0.84, 1.40) | 0.515 | 1.07 (0.82, 1.38) | 0.596 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | 0.94 (0.48, 1.84) | 0.848 | 0.94 (0.47, 1.88) | 0.862 | 0.89 (0.44, 1.80) | 0.747 |
| <32 (n=268; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 0.93 (0.74, 1.17) | 0.534 | 0.95 (0.70, 1.28) | 0.543 | 0.93 (0.68, 1.27) | 0.507 |
| Stroop test condition 1 | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | 1.61 (0.60, 4.31) | 0.259 | 1.71 (0.59, 4.96) | 0.270 | 1.89 (0.61, 5.86) | 0.226 |
| <15 (n=184; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.24 (0.97, 1.61) | 0.170 | 1.21 (0.92, 1.58) | 0.231 | 1.27 (0.94, 1.69) | 0.174 |
| ODI (events/h) | | | | | | |
| ≥15 (n=172) | 1.30 (0.40, 2.69) | 0.865 | 0.98 (0.34, 2.80) | 0.996 | 1.25 (0.45, 3.86) | 0.683 |
| <15 (n=186; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.29 (0.99, 1.68) | 0.140 | 1.27 (0.94, 1.69) | 0.178 | 1.33 (0.96, 1.84) | 0.139 |
| Mean SpO ₂ (%) | | | | | | |
| ≤92.5 (n=88) | 3.95 (1.54, 9.96) | 0.004 | 4.33 (1.57, 11.90) | 0.004 | 4.64 (1.52, 14.15) | 0.007 |
| >92.5 (n=270; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit decrease) | 1.24 (1.00, 1.42) | 0.088 | 1.23 (0.96, 1.43) | 0.092 | 1.26 (0.96, 1.47) | 0.103 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | 2.05 (0.79, 5.27) | 0.131 | 2.32 (0.80, 6.71) | 0.134 | 2.64 (0.81, 8.62) | 0.132 |
| <4.5 (n=266; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit increase) | 1.01 (0.98, 1.04) | 0.708 | 1.01 (0.97, 1.04) | 0.846 | 1.01 (0.97, 1.04) | 0.872 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | 1.29 (0.45, 3.64) | 0.636 | 1.44 (0.50, 4.15) | 0.500 | 1.48 (0.49, 4.49) | 0.487 |
| >72 (n=271; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit decrease) | 1.12 (0.72, 1.68) | 0.595 | 1.14 (0.74, 1.71) | 0.540 | 1.16 (0.72, 1.77) | 0.537 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | 1.29 (0.45, 3.72) | 0.636 | 1.40 (0.46, 4.23) | 0.555 | 1.65 (0.48, 5.67) | 0.423 |
| <32 (n=268; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.09 (0.75, 1.60) | 0.840 | 1.12 (0.74, 1.66) | 0.799 | 1.23 (0.76, 2.00) | 0.624 |
| Stroop test condition 2 | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | 1.59 (0.68, 3.71) | 0.295 | 1.47 (0.59, 3.65) | 0.423 | 1.46 (0.59, 3.61) | 0.428 |
| <15 (n=184; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.19 (0.98, 1.44) | 0.086 | 1.18 (0.95, 1.47) | 0.130 | 1.19 (0.95, 1.49) | 0.120 |
| ODI (events/h) | | | | | | |
| ≥15 (n=172) | 0.93 (0.40, 2.13) | 0.857 | 0.79 (0.33, 1.96) | 0.608 | 0.80 (0.32, 2.00) | 0.630 |
| <15 (n=186; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.19 (0.97, 1.49) | 0.093 | 1.19 (0.94, 1.51) | 0.141 | 1.21 (0.94, 1.52) | 0.136 |
| Mean SpO ₂ (%) | | | | | | |

| | | | | | | |
|--------------------------------|-------------------|-------|-------------------|-------|-------------------|-------|
| ≤92.5 (n=88) | 1.75 (0.75, 4.09) | 0.194 | 1.63 (0.67, 3.92) | 0.280 | 1.66 (0.67, 4.09) | 0.270 |
| >92.5 (n=270; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit decrease) | 1.06 (0.81, 1.26) | 0.615 | 1.02 (0.81, 1.24) | 0.870 | 1.02 (0.72, 1.25) | 0.875 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | 1.43 (0.61, 3.34) | 0.412 | 1.25 (0.50, 3.08) | 0.635 | 1.17 (0.45, 3.02) | 0.743 |
| <4.5 (n=266; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit increase) | 1.00 (0.97, 1.03) | 0.915 | 1.00 (0.97, 1.03) | 0.968 | 1.00 (0.97, 1.03) | 0.910 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | 0.75 (0.28, 2.01) | 0.562 | 0.70 (0.26, 1.92) | 0.492 | 0.69 (0.25, 1.90) | 0.468 |
| >72 (n=271; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit decrease) | 0.89 (0.57, 1.33) | 0.601 | 0.86 (0.56, 1.29) | 0.482 | 0.84 (0.54, 1.27) | 0.429 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | 2.66 (1.12, 6.34) | 0.027 | 2.55 (1.04, 6.26) | 0.041 | 2.58 (1.02, 6.54) | 0.046 |
| <32 (n=268; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.44 (1.08, 1.91) | 0.012 | 1.45 (1.07, 1.97) | 0.016 | 1.41 (1.08, 1.74) | 0.013 |
| Stroop test condition 3 | | | | | | |
| AHI (events/h) | | | | | | |
| ≥15 (n=174) | 0.80 (0.33, 1.91) | 0.594 | 0.56 (0.21, 1.48) | 0.218 | 0.57 (0.21, 1.52) | 0.228 |
| <15 (n=184; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 0.95 (0.75, 1.21) | 0.704 | 0.86 (0.66, 1.13) | 0.265 | 0.85 (0.65, 1.12) | 0.242 |
| ODI (events/h) | | | | | | |
| ≥15 (n=172) | 0.84 (0.36, 1.95) | 0.638 | 0.54 (0.21, 1.41) | 0.192 | 0.56 (0.21, 1.46) | 0.216 |
| <15 (n=186; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 0.98 (0.77, 1.25) | 0.926 | 0.88 (0.66, 1.17) | 0.367 | 0.87 (0.65, 1.14) | 0.328 |
| Mean SpO ₂ (%) | | | | | | |
| ≤92.5 (n=88) | 2.34 (1.01, 5.45) | 0.051 | 1.93 (0.78, 4.77) | 0.161 | 2.07 (0.82, 5.19) | 0.125 |
| >92.5 (n=270; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit decrease) | 1.06 (0.81, 1.26) | 0.565 | 0.98 (0.69, 1.22) | 0.922 | 0.98 (0.68, 1.22) | 0.916 |
| TST90 (%) | | | | | | |
| ≥4.5 (n=92) | 1.09 (0.45, 2.69) | 0.858 | 0.90 (0.34, 2.40) | 0.830 | 0.90 (0.33, 2.49) | 0.847 |
| <4.5 (n=266; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (1-unit increase) | 1.00 (0.98, 1.03) | 0.812 | 0.99 (0.97, 1.02) | 0.713 | 0.99 (0.97, 1.02) | 0.688 |
| Sleep efficiency (%) | | | | | | |
| ≤72 (n=87) | 1.56 (0.64, 3.80) | 0.329 | 1.52 (0.61, 3.80) | 0.370 | 1.56 (0.62, 3.92) | 0.348 |
| >72 (n=271; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit decrease) | 1.34 (0.90, 1.79) | 0.159 | 1.14 (0.86, 1.76) | 0.233 | 1.25 (0.86, 1.77) | 0.228 |
| Arousal index (events/h) | | | | | | |
| ≥32 (n=90) | 1.14 (0.45, 2.89) | 0.774 | 1.13 (0.43, 3.02) | 0.799 | 1.07 (0.39, 2.95) | 0.888 |
| <32 (n=268; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.05 (0.78, 1.42) | 0.771 | 0.99 (0.72, 1.34) | 0.920 | 0.98 (0.71, 1.33) | 0.874 |

Data are presented as adjusted odds ratio (OR) and 95% confidence interval (CI). Data were analyzed by multivariable logistic regression models using incidence of significant cognitive decline as dependent variable and each obstructive sleep apnoea parameter as independent variable. Bold text indicates significant results ($P < 0.01$). Model 1 = adjusted for age (continuous), sex (male, female), education (≥high school, <high school) and apolipoprotein E4 (carriers, non-carriers). Model 2 = model 1 additionally adjusted for body mass index (continuous), diabetes (yes, no), hypertension (yes, no), smoking (former or current, never), alcohol consumption (≥14, <14 units/week) and psychotropic drugs (yes, no). Model 3 = model 2 additionally adjusted for depression (yes, no), Epworth sleepiness scale (continuous), continuous positive airway pressure (yes, no) and chronic obstructive pulmonary disease (yes, no). Abbreviations: AHI = apnoea-hypopnoea index; CERAD = Consortium to Establish a Registry for Alzheimer's Disease; Cont. = continuous; FCSRT = Free and Cued Selective Reminding Test; MMSE = Mini-Mental State Examination; ODI = oxygen desaturation index; ref. = reference group; SpO₂ = oxygen saturation; TST90 = sleep time with oxygen saturation <90%.

Table S5. Baseline characteristics by age.

| | Age 65-74 years (n=289) | Age ≥75 years (n=69) | Test | P |
|--|----------------------------|-------------------------|-----------------|------------------|
| Clinical characteristics | | | | |
| Age, years | 69.4 ± 2.6 | 77.7 ± 2.3 | t = 24.3 | <0.001 |
| Men, n (%) | 122 (42.2) | 30 (43.5) | $\chi^2 = 0.0$ | 0.849 |
| ApoE4 carriers, n (%) | 68 (23.5) | 15 (21.7) | $\chi^2 = 0.1$ | 0.752 |
| Education (≥high school), n (%) | 121 (41.9) | 29 (42.0) | $\chi^2 = 0.0$ | 0.981 |
| BMI, kg/m ² | 26.9 ± 4.6 | 26.5 ± 4.0 | t = 0.6 | 0.526 |
| Diabetes, n (%) | 44 (15.2) | 10 (14.5) | $\chi^2 = 0.0$ | 0.879 |
| Hypertension, n (%) | 185 (64.0) | 51 (73.9) | $\chi^2 = 2.4$ | 0.119 |
| Smoking, n (%) | 162 (56.1) | 37 (53.6) | $\chi^2 = 0.13$ | 0.715 |
| Alcohol (≥14 units/week), n (%) | 53 (18.3) | 12 (17.4) | $\chi^2 = 0.0$ | 0.854 |
| Psychotropic drugs, n (%) | 47 (16.3) | 20 (29.0) | $\chi^2 = 5.9$ | 0.015 |
| Epworth Sleepiness Scale, points | 5.3 ± 3.4 | 4.6 ± 3.1 | t = 1.5 | 0.134 |
| Depression, n (%) | 118 (40.8) | 20 (29.0) | $\chi^2 = 3.3$ | 0.069 |
| CPAP, n (%) | 7 (2.4) | 1 (1.4) | Fisher | 1.000 |
| COPD, n (%) | 5 (1.7) | 5 (7.2) | Fisher | 0.026 |
| Sleep characteristics | | | | |
| AHI, events/h | 14.0 [0.0, 135.1] | 16.1 [0.6, 84.9] | U = 9553 | 0.589 |
| ODI, events/h | 13.6 [0.1, 121.3] | 14.3 [0.8, 80.8] | U = 9663 | 0.691 |
| Mean SpO ₂ , % | 93.5 ± 1.6 | 93.2 ± 1.7 | t = 1.18 | 0.264 |
| TST90, % | 0.8 [0.0, 91.9] | 1.3 [0.0, 69.4] | U = 8636 | 0.082 |
| Hypoxic burden, %min/h | 19.3 [0.1, 269.3] | 20.1 [0.7, 177.9] | U = 8575 | 0.515 |
| Sleep efficiency, % | 81.9 [31.4, 96.2] | 80.3 [29.6, 96.6] | U = 9313 | 0.395 |
| Arousal index, events/h | 22.5 [4.4, 104.6] | 24.9 [6.3, 60.2] | U = 9097 | 0.258 |
| Cognitive characteristics | | | | |
| MMSE, points | 30.0 [22.0, 30.0] | 30.0 [25.0, 30.0] | U = 8949 | 0.376 |
| Phonemic fluency, points | 21.8 ± 7.9 | 20.7 ± 8.8 | t = 0.9 | 0.347 |
| Semantic fluency, points | 31.3 ± 8.3 | 29.5 ± 8.5 | t = 1.5 | 0.115 |
| FCSRT delayed free recall, points | 12.1 ± 2. | 11.0 ± 2.6 | t = 3.0 | 0.002 |
| FCSRT delayed total recall, points | 16.0 [12.0, 16.0] | 16.0 [10.0, 16.0] | U = 8152 | 0.065 |
| DO-40 naming test, points | 40.0 [24.0, 40.0] | 40.0 [37.0, 40.0] | U = 8510 | 0.077 |
| CERAD constructional praxis task, points | 11.0 [7.0, 11.0] | 11.0 [5.0, 11.0] | U = 9791 | 0.805 |
| Stroop test condition 1, seconds | 16.0 ± 6.0 | 18.0 ± 7.4 | t = 2.2 | 0.025 |
| Stroop test condition 2, seconds | 20.3 ± 5.6 | 23.8 ± 9.0 | t = 4.0 | <0.001 |
| Stroop test condition 3, seconds | 32.0 ± 11.5 | 36.6 ± 13.6 | t = 2.8 | 0.005 |

Data are presented as mean ± standard deviation, median [range] or number of participants (%). Data were analysed using unpaired T-test (t), Mann-Whitney U test (U), chi-squared test (χ^2) or Fisher's exact test. Bold text indicates significant results (P <0.05). Abbreviations: AHI = apnoea-hypopnoea index; ApoE4 = apolipoprotein E4; BMI = body mass index; CERAD = Consortium to Establish a Registry for Alzheimer's Disease; COPD = chronic obstructive pulmonary disease; CPAP = continuous positive airway pressure; FCSRT = Free and Cued Selective Reminding Test; MMSE = Mini-Mental State Examination; ODI = oxygen desaturation index; SpO₂ = oxygen saturation; TST90 = sleep time with oxygen saturation <90%.

Table S6. Baseline characteristics by sex.

| | Men (n=152) | Women (n=206) | Test | P |
|--|-------------------|-------------------|-----------------|------------------|
| Clinical characteristics | | | | |
| Age, years | 71.0 ± 4.2 | 71.0 ± 4.1 | t = 0.1 | 0.895 |
| ApoE4 carriers, n (%) | 38 (25.0) | 45 (21.8) | $\chi^2 = 0.5$ | 0.484 |
| Education (≥high school), n (%) | 77 (50.6) | 73 (35.4) | $\chi^2 = 8.3$ | 0.004 |
| BMI, kg/m ² | 27.2 ± 3.6 | 26.5 ± 5.0 | t = 1.5 | 0.146 |
| Diabetes, n (%) | 33 (21.7) | 21 (10.2) | $\chi^2 = 9.1$ | 0.003 |
| Hypertension, n (%) | 112 (73.6) | 124 (60.2) | $\chi^2 = 7.1$ | 0.008 |
| Smoking, n (%) | 105 (69.1) | 94 (45.6) | $\chi^2 = 19.5$ | <0.001 |
| Alcohol (≥14 units/week), n (%) | 54 (35.5) | 11 (5.3) | $\chi^2 = 53.6$ | <0.001 |
| Psychotropic drugs, n (%) | 18 (11.8) | 49 (23.7) | $\chi^2 = 8.2$ | 0.004 |
| Epworth Sleepiness Scale, points | 6.0 ± 3.6 | 4.5 ± 3.2 | t = 4.1 | <0.001 |
| Depression, n (%) | 44 (28.9) | 94 (45.6) | $\chi^2 = 10.3$ | 0.001 |
| CPAP, n (%) | 2 (1.3) | 6 (2.9) | Fisher | 0.475 |
| COPD, n (%) | 5 (3.3) | 5 (2.4) | Fisher | 0.429 |
| Sleep characteristics | | | | |
| AHI, events/h | 21.6 [0.6, 88.1] | 10.7 [0.0, 135.1] | U = 10230 | <0.001 |
| ODI, events/h | 20.4 [0.4, 84.4] | 11.3 [0.1, 121.3] | U = 10728 | <0.001 |
| Mean SpO ₂ , % | 93.6 ± 1.6 | 93.2 ± 1.7 | t = 1.9 | 0.054 |
| TST90, % | 1.5 [0.0, 91.9] | 0.6 [0.0, 85.0] | U = 13777 | 0.051 |
| Hypoxic burden, %min/h | 29.6 [0.1, 269.3] | 14.4 [0.1, 177.8] | U = 10750 | <0.001 |
| Sleep efficiency, % | 77.6 [29.6, 96.1] | 83.4 [31.4, 96.6] | U = 11337 | <0.001 |
| Arousal index, events/h | 27.0 [4.4, 104.6] | 20.5 [4.9, 76.9] | U = 10302 | <0.001 |
| Cognitive characteristics | | | | |
| MMSE, points | 30.0 [20.0, 30.0] | 30.0 [23.0, 30.0] | U = 12595 | 0.007 |
| Phonemic fluency, points | 20.9 ± 8.1 | 22.0 ± 8.0 | t = 1.2 | 0.217 |
| Semantic fluency, points | 31.5 ± 8.5 | 30.8 ± 8.2 | t = 0.2 | 0.845 |
| FCSRT delayed free recall, points | 11.5 ± 2.3 | 12.1 ± 2.5 | t = 2.4 | 0.014 |
| FCSRT delayed total recall, points | 16.0 [10.0, 16.0] | 16.0 [11.0, 16.0] | U = 13333 | 0.182 |
| DO-40 naming test, points | 40.0 [24.0, 40.0] | 40.0 [37.0, 40.0] | U = 13923 | 0.468 |
| CERAD constructional praxis task, points | 11.0 [5.0, 11.0] | 11.0 [7.0, 11.0] | U = 15507 | 0.950 |
| Stroop test condition 1, seconds | 16.3 ± 6.9 | 16.4 ± 5.8 | t = 1.0 | 0.956 |
| Stroop test condition 2, seconds | 21.4 ± 5.7 | 20.7 ± 7.2 | t = 0.9 | 0.350 |
| Stroop test condition 3, seconds | 33.0 ± 13.3 | 32.7 ± 11.2 | t = 0.2 | 0.833 |

Data are presented as mean ± standard deviation, median [range] or number of participants (%). Data were analysed using unpaired T-test (t), Mann-Whitney U test (U), chi-squared test (χ^2) or Fisher's exact test. Bold text indicates significant results (P < 0.05). Abbreviations: AHI = apnoea-hypopnoea index; ApoE4 = apolipoprotein E4; BMI = body mass index; CERAD = Consortium to Establish a Registry for Alzheimer's Disease; COPD = chronic obstructive pulmonary disease; CPAP = continuous positive airway pressure; FCSRT = Free and Cued Selective Reminding Test; MMSE = Mini-Mental State Examination; ODI = oxygen desaturation index; SpO₂ = oxygen saturation; TST90 = sleep time with oxygen saturation <90%.

Table S7. Baseline characteristics by apolipoprotein E4 status.

| | ApoE4 non-carriers (n=275) | ApoE4 carriers (n=83) | Test | P |
|--|-------------------------------|--------------------------|----------------|-------|
| Clinical characteristics | | | | |
| Age, years | 71.1 ± 4.3 | 70.7 ± 3.8 | t = 0.7 | 0.500 |
| Men, n (%) | 114 (41.5) | 38 (45.8) | $\chi^2 = 0.5$ | 0.484 |
| Education (≥high school), n (%) | 112 (40.7) | 38 (45.8) | $\chi^2 = 0.6$ | 0.413 |
| BMI, kg/m ² | 26.9 ± 4.5 | 26.5 ± 4.7 | t = 0.6 | 0.523 |
| Diabetes, n (%) | 46 (16.7) | 8 (9.6) | $\chi^2 = 2.5$ | 0.114 |
| Hypertension, n (%) | 181 (65.8) | 55 (66.3) | $\chi^2 = 0.0$ | 0.940 |
| Smoking, n (%) | 153 (55.6) | 46 (55.4) | $\chi^2 = 0.0$ | 0.972 |
| Alcohol (≥14 units/week), n (%) | 43 (15.6) | 22 (26.5) | $\chi^2 = 5.1$ | 0.024 |
| Psychotropic drugs, n (%) | 54 (19.6) | 13 (15.7) | $\chi^2 = 0.6$ | 0.416 |
| Epworth Sleepiness Scale, points | 5.2 ± 3.3 | 5.1 ± 3.7 | t = 0.1 | 0.883 |
| Depression, n (%) | 101 (36.7) | 37 (44.6) | $\chi^2 = 1.6$ | 0.198 |
| CPAP, n (%) | 6 (2.2) | 2 (2.4) | Fisher | 1.000 |
| COPD, n (%) | 9 (3.3) | 1 (1.2) | Fisher | 0.284 |
| Sleep characteristics | | | | |
| AHI, events/h | 14.2 [0.6, 135.1] | 13.3 [0.0, 88.1] | U = 11334 | 0.924 |
| ODI, events/h | 13.7 [0.5, 121.3] | 14.8 [0.1, 84.4] | U = 11229 | 0.824 |
| Mean SpO ₂ , % | 93.4 ± 1.6 | 93.3 ± 1.6 | t = 0.8 | 0.434 |
| TST90, % | 0.9 [0.0, 91.9] | 0.7 [0.0, 85.0] | U = 11060 | 0.668 |
| Hypoxic burden, %min/h | 18.6 [0.1, 269.3] | 20.2 [0.8, 268.2] | U = 10326 | 0.923 |
| Sleep efficiency, % | 80.9 [29.6, 96.6] | 81.9 [57.8, 96.2] | U = 11259 | 0.853 |
| Arousal index, events/h | 23.1 [4.4, 104.6] | 22.5 [4.9, 76.9] | U = 10651 | 0.357 |
| Cognitive characteristics | | | | |
| MMSE, points | 30.0 [22.0, 30.0] | 30.0 [23.0, 30.0] | U = 9678 | 0.157 |
| Phonemic fluency, points | 21.4 ± 8.2 | 22.2 ± 7.7 | t = 0.8 | 0.442 |
| Semantic fluency, points | 31.0 ± 8.7 | 30.7 ± 6.9 | t = 0.2 | 0.779 |
| FCSRT delayed free recall, points | 11.8 ± 2.5 | 12.1 ± 2.4 | t = 1.1 | 0.276 |
| FCSRT delayed total recall, points | 16.0 [10.0, 16.0] | 16.0 [13.0, 16.0] | U = 9570 | 0.276 |
| DO-40 naming test, points | 40.0 [24.0, 40.0] | 40.0 [37.0, 40.0] | U = 10025 | 0.862 |
| CERAD constructional praxis task, points | 11.0 [5.0, 11.0] | 11.0 [6.0, 11.0] | U = 10739 | 0.315 |
| Stroop test condition 1, seconds | 16.4 ± 6.5 | 16.0 ± 5.9 | t = 0.5 | 0.633 |
| Stroop test condition 2, seconds | 21.2 ± 6.9 | 20.4 ± 5.3 | t = 0.8 | 0.380 |
| Stroop test condition 3, seconds | 32.6 ± 11.1 | 33.8 ± 14.8 | t = 0.8 | 0.481 |

Data are presented as mean ± standard deviation, median [range] or number of participants (%). Data were analysed using unpaired T-test (t), Mann-Whitney U test (U), chi-squared test (χ^2) or Fisher's exact test. Abbreviations: AHI = apnoea-hypopnoea index; ApoE4 = apolipoprotein E4; BMI = body mass index; CERAD = Consortium to Establish a Registry for Alzheimer's Disease; COPD = chronic obstructive pulmonary disease; CPAP = continuous positive airway pressure; FCSRT = Free and Cued Selective Reminding Test; MMSE = Mini-Mental State Examination; ODI = oxygen desaturation index; SpO₂ = oxygen saturation; TST90 = sleep time with oxygen saturation <90%.

Table S8. Associations between apnoea-hypopnoea index and annual change in cognitive scores (sensitivity analysis).

| | Annual change in cognitive scores | | | | | |
|---|-----------------------------------|-------|---------------|-------|---------------|-------|
| | Model 1 | | Model 2 | | Model 3 | |
| | <i>B</i> (SE) | P | <i>B</i> (SE) | P | <i>B</i> (SE) | P |
| MMSE | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | -0.02 (0.04) | 0.583 | -0.02 (0.04) | 0.574 | -0.02 (0.04) | 0.535 |
| <20 (n=223; ref.) | | | | | | |
| ≥25 (n=103) | -0.06 (0.04) | 0.114 | -0.07 (0.04) | 0.097 | -0.07 (0.04) | 0.101 |
| <25 (n=255; ref.) | | | | | | |
| ≥30 (n=80) | 0.00 (0.04) | 0.920 | -0.01 (0.05) | 0.828 | -0.01 (0.05) | 0.808 |
| <30 (n=278; ref.) | | | | | | |
| Phonemic fluency | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | -0.25 (0.15) | 0.102 | -0.35 (0.16) | 0.028 | -0.34 (0.16) | 0.030 |
| <20 (n=223; ref.) | | | | | | |
| ≥25 (n=103) | -0.15 (0.17) | 0.373 | -0.23 (0.17) | 0.181 | -0.21 (0.17) | 0.209 |
| <25 (n=255; ref.) | | | | | | |
| ≥30 (n=80) | -0.14 (0.18) | 0.426 | -0.23 (0.18) | 0.202 | -0.22 (0.18) | 0.222 |
| <30 (n=278; ref.) | | | | | | |
| Semantic fluency | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | -0.07 (0.17) | 0.704 | -0.09 (0.18) | 0.635 | -0.08 (0.18) | 0.644 |
| <20 (n=223; ref.) | | | | | | |
| ≥25 (n=103) | -0.14 (0.19) | 0.459 | -0.15 (0.19) | 0.430 | -0.13 (0.20) | 0.504 |
| <25 (n=255; ref.) | | | | | | |
| ≥30 (n=80) | -0.22 (0.20) | 0.278 | -0.26 (0.21) | 0.218 | -0.25 (0.21) | 0.243 |
| <30 (n=278; ref.) | | | | | | |
| FCSRT delayed free recall | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | 0.02 (0.06) | 0.735 | 0.00 (0.07) | 0.998 | 0.00 (0.07) | 0.965 |
| <20 (n=223; ref.) | | | | | | |
| ≥25 (n=103) | 0.00 (0.07) | 0.958 | -0.01 (0.19) | 0.833 | -0.01 (0.07) | 0.912 |
| <25 (n=255; ref.) | | | | | | |
| ≥30 (n=80) | -0.01 (0.07) | 0.934 | -0.02 (0.08) | 0.782 | -0.01 (0.08) | 0.847 |
| <30 (n=278; ref.) | | | | | | |
| FCSRT delayed total recall | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | -0.01 (0.03) | 0.720 | -0.02 (0.04) | 0.670 | -0.01 (0.04) | 0.717 |
| <20 (n=223; ref.) | | | | | | |
| ≥25 (n=103) | -0.02 (0.04) | 0.523 | -0.02 (0.04) | 0.532 | -0.02 (0.04) | 0.642 |
| <25 (n=255; ref.) | | | | | | |
| ≥30 (n=80) | -0.01 (0.04) | 0.805 | -0.01 (0.04) | 0.871 | 0.000 (0.04) | 0.991 |
| <30 (n=278; ref.) | | | | | | |
| DO-40 naming test | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | 0.03 (0.03) | 0.379 | 0.02 (0.03) | 0.542 | 0.02 (0.03) | 0.579 |
| <20 (n=223; ref.) | | | | | | |
| ≥25 (n=103) | 0.01 (0.03) | 0.766 | 0.00 (0.03) | 0.951 | 0.00 (0.03) | 0.916 |
| <25 (n=255; ref.) | | | | | | |
| ≥30 (n=80) | 0.05 (0.03) | 0.170 | 0.04 (0.03) | 0.242 | 0.04 (0.03) | 0.305 |
| <30 (n=278; ref.) | | | | | | |
| CERAD constructional praxis task | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | -0.01 (0.03) | 0.743 | -0.01 (0.03) | 0.639 | -0.02 (0.03) | 0.611 |
| <20 (n=223; ref.) | | | | | | |

| | | | | | | |
|--------------------------------|--------------|-------|--------------|-------|--------------|-------|
| ≥25 (n=103) | 0.02 (0.03) | 0.617 | 0.01 (0.03) | 0.687 | 0.01 (0.03) | 0.728 |
| <25 (n=255; ref.) | | | | | | |
| ≥30 (n=80) | 0.03 (0.04) | 0.323 | 0.03 (0.04) | 0.352 | 0.03 (0.04) | 0.372 |
| <30 (n=278; ref.) | | | | | | |
| Stroop test condition 1 | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | 0.00 (0.15) | 0.986 | 0.02 (0.16) | 0.918 | 0.04 (0.16) | 0.816 |
| <20 (n=223; ref.) | | | | | | |
| ≥25 (n=103) | 0.05 (0.02) | 0.743 | 0.06 (0.02) | 0.716 | 0.08 (0.16) | 0.633 |
| <25 (n=255; ref.) | | | | | | |
| ≥30 (n=80) | 0.13 (0.17) | 0.471 | 0.15 (0.18) | 0.415 | 0.17 (0.18) | 0.326 |
| <30 (n=278; ref.) | | | | | | |
| Stroop test condition 2 | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | -0.10 (0.19) | 0.573 | -0.07 (0.19) | 0.714 | -0.05 (0.19) | 0.777 |
| <20 (n=223; ref.) | | | | | | |
| ≥25 (n=103) | -0.14 (0.20) | 0.483 | -0.12 (0.20) | 0.552 | -0.11 (0.20) | 0.596 |
| <25 (n=255; ref.) | | | | | | |
| ≥30 (n=80) | -0.18 (0.21) | 0.414 | -0.16 (0.22) | 0.463 | -0.14 (0.21) | 0.529 |
| <30 (n=278; ref.) | | | | | | |
| Stroop test condition 3 | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | -0.30 (0.33) | 0.354 | -0.32 (0.34) | 0.344 | -0.33 (0.34) | 0.330 |
| <20 (n=223; ref.) | | | | | | |
| ≥25 (n=103) | -0.68 (0.35) | 0.048 | -0.76 (0.36) | 0.034 | -0.76 (0.36) | 0.033 |
| <25 (n=255; ref.) | | | | | | |
| ≥30 (n=80) | -0.60 (0.37) | 0.112 | -0.65 (0.38) | 0.094 | -0.65 (0.39) | 0.090 |
| <30 (n=278; ref.) | | | | | | |

Data are presented as unstandardized beta coefficient (*B*) and standard error (SE). Data were analyzed by multivariable linear regression models using annual change in cognitive scores as dependent variable and apnoea-hypopnoea index as independent variable. Model 1 = adjusted for age (continuous), sex (male, female), education (≥high school, <high school) and apolipoprotein E4 (carriers, non-carriers). Model 2 = model 1 additionally adjusted for body mass index (continuous), diabetes (yes, no), hypertension (yes, no), smoking (former or current, never), alcohol consumption (≥14, <14 units/week) and psychotropic drugs (yes, no). Model 3 = model 2 additionally adjusted for depression (yes, no), Epworth Sleepiness Scale (continuous), continuous positive airway pressure (yes, no) and chronic obstructive pulmonary disease (yes, no). Abbreviations: AHI = apnoea-hypopnoea index; CERAD = Consortium to Establish a Registry for Alzheimer's Disease; FCSRT = Free and Cued Selective Reminding Test; MMSE = Mini-Mental State Examination; ref. = reference group.

Table S9. Associations between apnoea-hypopnoea index and incidence of significant cognitive decline (sensitivity analysis).

| | Incidence of significant cognitive decline | | | | | |
|---|--|-------|--------------------|--------------|-------------------|--------------|
| | Model 1 | | Model 2 | | Model 3 | |
| | OR (95% CI) | P | OR (95% CI) | P | OR (95% CI) | P |
| MMSE | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | 0.78 (0.39, 1.55) | 0.474 | 0.80 (0.38, 1.68) | 0.561 | 0.79 (0.38, 1.66) | 0.537 |
| <20 (n=223; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| ≥25 (n=103) | 1.04 (0.51, 2.11) | 0.921 | 1.11 (0.52, 2.35) | 0.794 | 1.09 (0.51, 2.33) | 0.825 |
| <25 (n=255; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| ≥30 (n=80) | 0.84 (0.37, 1.88) | 0.664 | 0.89 (0.38, 2.05) | 0.794 | 0.88 (0.38, 2.07) | 0.773 |
| <30 (n=278; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Phonemic fluency | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | 2.36 (1.22, 4.55) | 0.011 | 2.99 (1.46, 6.11) | 0.003 | 2.99 (1.46, 6.15) | 0.003 |
| <20 (n=223; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| ≥25 (n=103) | 1.94 (0.98, 3.87) | 0.058 | 2.32 (1.11, 4.82) | 0.024 | 2.27 (1.08, 4.77) | 0.030 |
| <25 (n=255; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| ≥30 (n=80) | 1.99 (0.95, 4.14) | 0.067 | 2.39 (1.10, 5.22) | 0.028 | 2.38 (1.08, 5.25) | 0.032 |
| <30 (n=278; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Semantic fluency | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | 1.19 (0.63, 2.25) | 0.598 | 1.23 (0.62, 2.42) | 0.554 | 1.21 (0.61, 2.40) | 0.576 |
| <20 (n=223; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| ≥25 (n=103) | 1.50 (0.77, 2.91) | 0.232 | 1.58 (0.78, 3.19) | 0.202 | 1.54 (0.76, 3.14) | 0.234 |
| <25 (n=255; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| ≥30 (n=80) | 1.78 (0.88, 3.58) | 0.107 | 1.88 (0.91, 3.92) | 0.090 | 1.87 (0.89, 3.92) | 0.097 |
| <30 (n=278; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| FCSRT delayed free recall | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | 1.39 (0.75, 2.57) | 0.290 | 1.33 (0.69, 2.54) | 0.394 | 1.35 (0.69, 2.61) | 0.378 |
| <20 (n=223; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| ≥25 (n=103) | 1.54 (0.80, 2.94) | 0.192 | 1.43 (0.72, 2.83) | 0.311 | 1.44 (0.71, 2.90) | 0.306 |
| <25 (n=255; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| ≥30 (n=80) | 1.44 (0.72, 2.88) | 0.293 | 1.34 (0.65, 2.76) | 0.430 | 1.33 (0.64, 2.79) | 0.447 |
| <30 (n=278; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| FCSRT delayed total recall | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | 1.77 (0.78, 3.99) | 0.170 | 1.81 (0.77, 4.22) | 0.173 | 1.79 (0.74, 4.19) | 0.199 |
| <20 (n=223; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| ≥25 (n=103) | 1.54 (0.70, 3.54) | 0.310 | 1.43 (0.60, 3.42) | 0.422 | 1.38 (0.57, 3.38) | 0.474 |
| <25 (n=255; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| ≥30 (n=80) | 1.29 (0.54, 3.12) | 0.564 | 1.15 (0.46, 2.90) | 0.765 | 1.08 (0.42, 2.76) | 0.877 |
| <30 (n=278; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| DO-40 naming test | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | 0.44 (0.15, 1.28) | 0.132 | 0.44 (0.15, 0.135) | 0.152 | 0.44 (0.14, 1.36) | 0.155 |
| <20 (n=223; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| ≥25 (n=103) | 0.70 (0.24, 2.05) | 0.511 | 0.74 (0.25, 2.28) | 0.599 | 0.76 (0.24, 2.42) | 0.649 |
| <25 (n=255; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| ≥30 (n=80) | 0.50 (0.14, 1.82) | 0.293 | 0.51 (0.13, 1.95) | 0.327 | 0.52 (0.13, 2.04) | 0.350 |
| <30 (n=278; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| CERAD constructional praxis task | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | 0.80 (0.43, 1.46) | 0.459 | 0.79 (0.42, 1.49) | 0.473 | 0.80 (0.42, 1.51) | 0.489 |
| <20 (n=223; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |

| | | | | | | |
|--------------------------------|-------------------|-------|-------------------|-------|-------------------|-------|
| ≥25 (n=103) | 0.57 (0.29, 1.13) | 0.110 | 0.56 (0.27, 1.14) | 0.110 | 0.53 (0.26, 1.11) | 0.093 |
| <25 (n=255; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| ≥30 (n=80) | 0.67 (0.32, 1.41) | 0.293 | 0.67 (0.32, 1.43) | 0.304 | 0.66 (0.30, 1.41) | 0.283 |
| <30 (n=278; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Stroop test condition 1 | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | 1.47 (0.57, 3.80) | 0.428 | 1.34 (0.48, 3.73) | 0.575 | 1.67 (0.56, 4.97) | 0.360 |
| <20 (n=223; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| ≥25 (n=103) | 1.36 (0.51, 3.67) | 0.538 | 1.21 (0.42, 3.46) | 0.721 | 1.37 (0.44, 4.26) | 0.590 |
| <25 (n=255; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| ≥30 (n=80) | 1.48 (0.52, 4.17) | 0.460 | 1.29 (0.43, 3.84) | 0.647 | 1.55 (0.49, 4.96) | 0.457 |
| <30 (n=278; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Stroop test condition 2 | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | 1.10 (0.48, 2.55) | 0.817 | 1.00 (0.41, 2.44) | 0.990 | 1.04 (0.43, 2.54) | 0.929 |
| <20 (n=223; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| ≥25 (n=103) | 1.17 (0.49, 2.79) | 0.729 | 1.10 (0.44, 2.74) | 0.844 | 1.05 (0.41, 2.70) | 0.917 |
| <25 (n=255; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| ≥30 (n=80) | 1.34 (0.54, 3.31) | 0.528 | 1.26 (0.49, 3.25) | 0.632 | 1.01 (0.99, 1.04) | 0.136 |
| <30 (n=278; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Stroop test condition 3 | | | | | | |
| AHI (events/h) | | | | | | |
| ≥20 (n=135) | 0.93 (0.40, 2.19) | 0.876 | 0.68 (0.26, 1.75) | 0.411 | 1.29 (0.49, 3.39) | 0.605 |
| <20 (n=223; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| ≥25 (n=103) | 0.96 (0.39, 2.37) | 0.938 | 0.67 (0.26, 1.76) | 0.423 | 0.71 (0.28, 1.81) | 0.471 |
| <25 (n=255; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| ≥30 (n=80) | 0.84 (0.31, 2.25) | 0.732 | 0.59 (0.21, 1.69) | 0.328 | 0.57 (0.19, 1.65) | 0.297 |
| <30 (n=278; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |

Data are presented as adjusted odds ratio (OR) and 95% confidence interval (CI). Data were analyzed by multivariable logistic regression models using incidence of significant cognitive decline as dependent variable and apnoea-hypopnoea index as independent variable. Bold text indicates significant results ($P < 0.01$). Model 1 = adjusted for age (continuous), sex (male, female), education (≥high school, <high school) and apolipoprotein E4 (carriers, non-carriers). Model 2 = model 1 additionally adjusted for body mass index (continuous), diabetes (yes, no), hypertension (yes, no), smoking (former or current, never), alcohol consumption (≥14, <14 units/week) and psychotropic drugs (yes, no). Model 3 = model 2 additionally adjusted for depression (yes, no), Epworth sleepiness scale (continuous), continuous positive airway pressure (yes, no) and chronic obstructive pulmonary disease (yes, no). Abbreviations: AHI = apnoea-hypopnoea index; CERAD = Consortium to Establish a Registry for Alzheimer's Disease; FCSRT = Free and Cued Selective Reminding Test; MMSE = Mini-Mental State Examination; ref. = reference group.

Table S10. Associations between hypoxic burden and annual change in cognitive scores (sensitivity analysis).

| | Annual change in cognitive scores | | | | | |
|---|-----------------------------------|-------|----------------|-------|----------------|-------|
| | Model 1 | | Model 2 | | Model 3 | |
| | <i>B</i> (SE) | P | <i>B</i> (SE) | P | <i>B</i> (SE) | P |
| MMSE | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | 0.010 (0.043) | 0.814 | 0.019 (0.044) | 0.663 | 0.013 (0.045) | 0.764 |
| <42 (n=257; ref.) | | | | | | |
| Cont. (10-unit increase) | -0.002 (0.005) | 0.735 | 0.000 (0.005) | 0.901 | 0.000 (0.005) | 0.879 |
| Phonemic fluency | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | -0.325 (0.177) | 0.067 | -0.328 (0.178) | 0.066 | -0.328 (0.178) | 0.065 |
| <42 (n=257; ref.) | | | | | | |
| Cont. (10-unit increase) | -0.026 (0.021) | 0.198 | -0.026 (0.021) | 0.201 | -0.027 (0.021) | 0.186 |
| Semantic fluency | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | -0.136 (0.201) | 0.500 | -0.109 (0.204) | 0.595 | -0.122 (0.205) | 0.551 |
| <42 (n=257; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.009 (0.023) | 0.700 | 0.014 (0.024) | 0.537 | 0.018 (0.024) | 0.457 |
| FCSRT delayed free recall | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | -0.040 (0.074) | 0.591 | -0.059 (0.075) | 0.438 | -0.043 (0.073) | 0.576 |
| <42 (n=257; ref.) | | | | | | |
| Cont. (10-unit increase) | -0.006 (0.009) | 0.461 | -0.009 (0.009) | 0.287 | -0.008 (0.009) | 0.319 |
| FCSRT delayed total recall | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | -0.016 (0.040) | 0.694 | -0.023 (0.040) | 0.572 | -0.012 (0.041) | 0.770 |
| <42 (n=257; ref.) | | | | | | |
| Cont. (10-unit increase) | -0.003 (0.005) | 0.523 | -0.004 (0.005) | 0.402 | -0.003 (0.005) | 0.518 |
| DO-40 naming test | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | 0.055 (0.034) | 0.103 | 0.049 (0.034) | 0.148 | 0.049 (0.034) | 0.152 |
| <42 (n=257; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.006 (0.004) | 0.096 | 0.006 (0.004) | 0.109 | 0.005 (0.004) | 0.146 |
| CERAD constructional praxis task | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | 0.008 (0.036) | 0.830 | 0.005 (0.036) | 0.895 | 0.005 (0.037) | 0.885 |
| <42 (n=257; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.003 (0.004) | 0.388 | 0.003 (0.004) | 0.477 | 0.003 (0.004) | 0.516 |
| Stroop test condition 1 | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | -0.027 (0.176) | 0.880 | -0.053 (0.180) | 0.767 | -0.016 (0.181) | 0.930 |
| <42 (n=257; ref.) | | | | | | |
| Cont. (10-unit increase) | 0.013 (0.020) | 0.493 | 0.011 (0.020) | 0.584 | 0.014 (0.020) | 0.469 |
| Stroop test condition 2 | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | -0.261 (0.218) | 0.232 | -0.268 (0.223) | 0.230 | -0.265 (0.226) | 0.242 |
| <42 (n=257; ref.) | | | | | | |
| Cont. (10-unit increase) | -0.010 (0.025) | 0.669 | -0.011 (0.025) | 0.673 | -0.008 (0.025) | 0.741 |
| Stroop test condition 3 | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | -0.519 (0.377) | 0.169 | -0.559 (0.384) | 0.146 | -0.605 (0.389) | 0.121 |
| <42 (n=257; ref.) | | | | | | |
| Cont. (10-unit increase) | -0.059 (0.042) | 0.164 | -0.065 (0.043) | 0.128 | -0.067 (0.044) | 0.120 |

Data are presented as unstandardized beta coefficient (*B*) and standard error (SE). Data were analyzed by multivariable linear regression models using annual change in cognitive scores as dependent variable and hypoxic burden as independent variable. Model

1 = adjusted for age (continuous), sex (male, female), education (\geq high school, $<$ high school) and apolipoprotein E4 (carriers, non-carriers). Model 2 = model 1 additionally adjusted for body mass index (continuous), diabetes (yes, no), hypertension (yes, no), smoking (former or current, never), alcohol consumption (≥ 14 , <14 units/week) and psychotropic drugs (yes, no). Model 3 = model 2 additionally adjusted for depression (yes, no), Epworth Sleepiness Scale (continuous), continuous positive airway pressure (yes, no) and chronic obstructive pulmonary disease (yes, no). Abbreviations: CERAD = Consortium to Establish a Registry for Alzheimer's Disease; FCSRT = Free and Cued Selective Reminding Test; MMSE = Mini-Mental State Examination; ref. = reference group.

Table S11. Associations between hypoxic burden and incidence of significant cognitive decline (sensitivity analysis).

| | Incidence of significant cognitive decline | | | | | |
|---|--|-------|-------------------|-------|-------------------|-------|
| | Model 1 | | Model 2 | | Model 3 | |
| | OR (95% CI) | P | OR (95% CI) | P | OR (95% CI) | P |
| MMSE | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | 1.12 (0.53, 2.36) | 0.765 | 1.12 (0.52, 2.42) | 0.774 | 1.08 (0.49, 2.37) | 0.854 |
| <42 (n=257; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.00 (0.92, 1.08) | 0.979 | 1.00 (0.92, 1.08) | 0.968 | 1.00 (0.91, 1.08) | 0.934 |
| Phonemic fluency | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | 2.16 (1.06, 4.40) | 0.033 | 2.31 (1.11, 4.82) | 0.025 | 2.26 (1.07, 4.79) | 0.033 |
| <42 (n=257; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.06 (0.98, 1.15) | 0.131 | 1.06 (0.98, 1.16) | 0.124 | 1.06 (0.98, 1.16) | 0.142 |
| Semantic fluency | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | 1.90 (0.95, 3.77) | 0.067 | 1.96 (0.96, 3.97) | 0.063 | 1.90 (0.92, 3.90) | 0.081 |
| <42 (n=257; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.02 (0.95, 1.10) | 0.548 | 1.02 (0.94, 1.10) | 0.675 | 1.01 (0.93, 1.11) | 0.754 |
| FCSRT delayed free recall | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | 1.68 (0.85, 3.31) | 0.134 | 1.59 (0.79, 3.19) | 0.192 | 1.45 (0.71, 2.96) | 0.308 |
| <42 (n=257; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.08 (1.00, 1.16) | 0.039 | 1.08 (1.00, 1.17) | 0.038 | 1.08 (1.00, 1.16) | 0.058 |
| FCSRT delayed total recall | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | 1.43 (0.60, 3.37) | 0.417 | 1.47 (0.61, 3.51) | 0.388 | 1.20 (0.48, 2.99) | 0.693 |
| <42 (n=257; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.04 (0.95, 1.14) | 0.397 | 1.04 (0.95, 1.14) | 0.381 | 1.04 (0.94, 1.15) | 0.430 |
| DO-40 naming test | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | 0.31 (0.07, 1.40) | 0.127 | 0.31 (0.07, 1.46) | 0.139 | 0.32 (0.07, 1.50) | 0.147 |
| <42 (n=257; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 0.94 (0.81, 1.09) | 0.417 | 0.95 (0.82, 1.10) | 0.509 | 0.95 (0.82, 1.17) | 0.567 |
| CERAD constructional praxis task | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | 0.74 (0.36, 1.52) | 0.421 | 0.76 (0.37, 1.57) | 0.454 | 0.69 (0.33, 1.45) | 0.330 |
| <42 (n=257; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 0.97 (0.89, 1.05) | 0.452 | 0.97 (0.89, 1.06) | 0.550 | 0.97 (0.89, 1.05) | 0.442 |
| Stroop test condition 1 | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | 1.62 (0.56, 4.64) | 0.370 | 1.38 (0.46, 4.11) | 0.562 | 1.66 (0.52, 5.30) | 0.388 |
| <42 (n=257; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.06 (0.97, 1.17) | 0.206 | 1.05 (0.94, 1.16) | 0.382 | 1.06 (0.95, 1.18) | 0.276 |
| Stroop test condition 2 | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | 1.15 (0.45, 2.95) | 0.774 | 1.06 (0.40, 2.80) | 0.898 | 0.96 (0.35, 2.59) | 0.929 |
| <42 (n=257; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.05 (0.96, 1.14) | 0.301 | 1.04 (0.95, 1.14) | 0.406 | 1.03 (0.94, 1.14) | 0.460 |
| Stroop test condition 3 | | | | | | |
| Hypoxic burden (%min/h) | | | | | | |
| ≥42 (n=83) | 1.19 (0.46, 3.06) | 0.723 | 1.08 (0.41, 2.88) | 0.874 | 0.85 (0.30, 2.39) | 0.760 |
| <42 (n=257; ref.) | 1 (ref.) | | 1 (ref.) | | 1 (ref.) | |
| Cont. (10-unit increase) | 1.01 (0.91, 1.17) | 0.885 | 0.99 (0.89, 1.09) | 0.842 | 0.98 (0.88, 1.08) | 0.653 |

Data are presented as adjusted odds ratio (OR) and 95% confidence interval (CI). Data were analyzed by multivariable logistic regression models using incidence of significant cognitive decline as dependent variable and hypoxic burden as independent

variable. Model 1 = adjusted for age (continuous), sex (male, female), education (\geq high school, $<$ high school) and apolipoprotein E4 (carriers, non-carriers). Model 2 = model 1 additionally adjusted for body mass index (continuous), diabetes (yes, no), hypertension (yes, no), smoking (former or current, never), alcohol consumption (≥ 14 , <14 units/week) and psychotropic drugs (yes, no). Model 3 = model 2 additionally adjusted for depression (yes, no), Epworth sleepiness scale (continuous), continuous positive airway pressure (yes, no) and chronic obstructive pulmonary disease (yes, no). Abbreviations: CERAD = Consortium to Establish a Registry for Alzheimer's Disease; FCSRT = Free and Cued Selective Reminding Test; MMSE = Mini-Mental State Examination; ref. = reference group.

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