BENESCO
Bern Network Epilepsy Sleep Consciousness

"Sleep characteristics and cognition in the general population: results from the HypnoLaus study"

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Plan

1. The HypnoLaus cohort study
2. Sleep characteristics of the general population
    1. Effects of age, gender, socioeconomic status, noise and Moon phase on sleep
    2. Prevalence of sleep disorders in the general population
        1. Insomnia and hypnotics
        2. Sleep disordered breathing
        3. Periodic leg movements
        4. REM sleep behavior disorder
3. Sleep and cognition
    1. Cross-sectional analysis
    2. Prospective studies

THE HYPNOLAUS COHORT STUDY

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CoLaus/PsychoLaus cohort

- Population-based cohort study of 6'738 participants living in Lausanne
- Representative of the adult population of Lausanne:
  - The distribution of age groups, gender, and zip codes of participants were similar to the source population
- Recruitment period : 2003-2006
- Aged 35-75 years

CoLaus/PsychoLaus cohort

- The main goals of the CoLaus/PsycoLaus were to obtain information on:

1) The prevalence of cardiovascular and psychiatric diseases and risk factors in Lausanne population

2) New genetic determinants of these factors

CoLaus/PsychoLaus cohort

- All subjects had a comprehensive genetic and cardiovascular risk profile assessment including:
  - Medical history
  - Biometric measurements
  - Laboratory tests:
    1) Markers of diabetes and insulin resistance
    2) Makers of dyslipidemia
    3) Markers associated with increased CVD risk
    4) Markers of co-morbid conditions (liver and renal function tests,…)

- 4000 had an extensive psychiatric evaluation

CoLaus/PsycoLaus

CoLaus cohort

2003 — 2006

Representative sample of the adult population of Lausanne
6738 participants
genetic and cardiovascular risk profile
4000 psychiatric evaluation

CoLaus/PsycoLaus follow-up

Representative sample of the adult population of Lausanne
6738 participants
genetic and cardiovascular risk profile
4000 psychiatric evaluation

Re-evaluation

CoLaus/PsychoLaus II - HypnoLaus

- **HypnoLaus** 2009-2013

- The main questions HypnoLaus will try to answer are:

  1) What are the sleep characteristics and what is the prevalence of sleep disorders in a middle aged general population?

  2) What are the genetic determinants of sleep regulation and sleep disorders?

  3) Is there any association between sleep disorders, cardiovascular, metabolic and neuro-psychiatric disorders?

Colaus II - HypnoLaus

- 5064 participants of the CoLaus/PsychoLaus study completed various sleep questionnaires regarding their sleep habits and potential sleep disorders
  - Pittsburgh sleep quality index (PSQI)
  - Epworth sleepiness scale (Daytime sleepiness)
  - Horne-Ostberg (Chronotype)
  - Ullanlina (Narcolepsy)
  - Berlin (Sleep apnea)
  - Restless legs syndrome (IRSSG diagnosic criteria and severity)
  - Munich (Parasomnia)

- 2168 had a full PSG at home

Polysomnography

- Electroencephalograms (EEG) from frontal, central and occipital areas
- Electro-oculograms (EOG)
- Submental electromyogram (EMG)
- Respiratory airflow (nasal cannula)
- Thoracic and abdominal movements
- Pulse oximetry
- Electrocardiogram (EKG)
- Body position
- Right and left leg EMG

Polysomnography

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- Body position
- Right and left leg EMG

Supplementary Table S1. *Comparisons between HypnoLaus and CoLaus (follow-up at 5 years) samples*

General population

	CoLaus[#]	HypnoLaus[#]	Cohen's d*	P value*
N	5064	2121		
Age, yrs (mean ± SD)	57·8 ± 10·5	57·6 ± 10·5 [(1)]	0·02	0·404
Male gender (%)	46·5	48·3	NA	0·034
BMI, kg/m^2 (mean ± SD)	26·2 ± 4·6	26·2 ± 4·4	0·00	0·934
ESS (mean ± SD)	5·8 ± 3·8	6·2 ± 3·9	-0·20	<0·001
BQ (mean ± SD)	0·89 ± 0·81	0·96 ± 0·83	-0·13	<0·001
PSQI (mean ± SD)	4·99 ± 3·21	5·14 ± 3·29	-0·08	0·008

*[#]HypnoLaus sample nested in CoLaus (follow-up at 5 years) sample. (1) Age at sampling time. *Comparison between HypnoLaus sample (who underwent PSG) and non-HypnoLaus (no PSG) sample (t-test). BMI: body mass index; ESS: Epworth Sleepiness Scale; BQ: Berlin Questionnaire; PSQI: Pittsburgh Sleep Quality Index.*

R Heinzer, Lancet Respir Med 2015

SLEEP CHARACTERISTICS OF THE GENERAL POPULATION

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Summary of participants characteristics

Parameter	Value
n	**2168**
Age (y)	57.6 ± 10.5
Gender	48.3 % males
Body mass index (kg/m^2)	26.2 ± 4.4
Neck circumference	36.7 ± 4.7
Mallampati score	2.5 ± 1.4
Epworth sleepiness scale score	6.2 ± 3.9
PSQI	5.14 ± 3.29

Summary of polysomnography results*

Parameter	Value
Total sleep time (h)	6.7 ± 1.2
Sleep efficiency (%)	85.3 ± 10.7
Sleep latency (min)	17.7 ± 23.4
WASO (min)	70.8 ± 55.6
Arousal index (n/h)	20.1 ± 10.2

* Sleep and arousals were scored based on the 2007 AASM Manual

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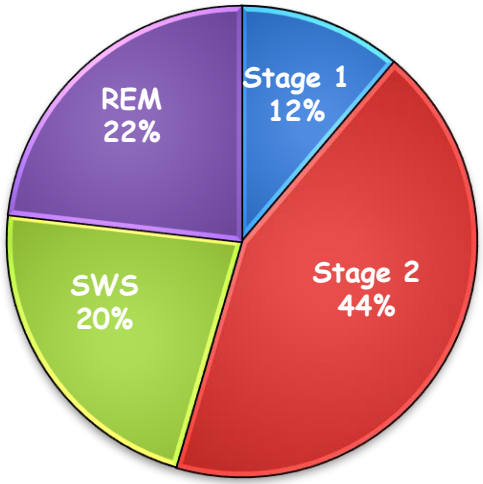
Sleep stages



* Sleep and arousals were scored based on the 2007 AASM Manual

Summary of polysomnography results*

Parameter	Value
Total sleep time (h)	6.7 ± 1.2
Sleep efficiency (%)	85.3 ± 10.7
Sleep latency (min)	17.7 ± 23.4
WASO (min)	70.8 ± 55.6
Arousal index (n/h)	20.1 ± 10.2
Apnea/hypopnea index (n/h)	Median (25^{th}–75^{th} percentiles)
• Chicago (AASM 1999) criteria	10.8 (4.8 – 22.0)
• AASM 2007 criteria	4.3 (1.2 – 11.1)
• AASM 2013 criteria	9.9 (4.2 – 20.6)
PLMS (n/h)	2 (0-64)

*PLMS were scored according to WASM criteria

EFFECT OF AGE, SEX, SOCIO-ECONOMIC STATUS, NOIS AND MOON ON SLEEP

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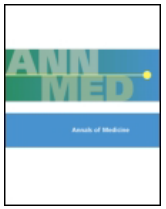
Age and gender variations of sleep in subjects without sleep disorders



Gianina Luca, José Haba Rubio, Daniela Andries, Nadia Tobback, Peter Vollenweider, Gérard Waeber, Pedro Marques Vidal, Martin Preisig, Raphaël Heinzer & Mehdi Tafti

Selection of subjects without sleep complaints:

1) A "non-complaining" population based on information from PSQI:

Subjects who declared sleep complaints (mainly environmental such as noise including the partner's snoring, personal or job-related stressors, N=418), shift workers (N=30), those taking any sleep medication (N=985), and those reporting the presence of sleep disorders (N=933): **2966 participants.**

2) For the polysomnographic data were excluded:

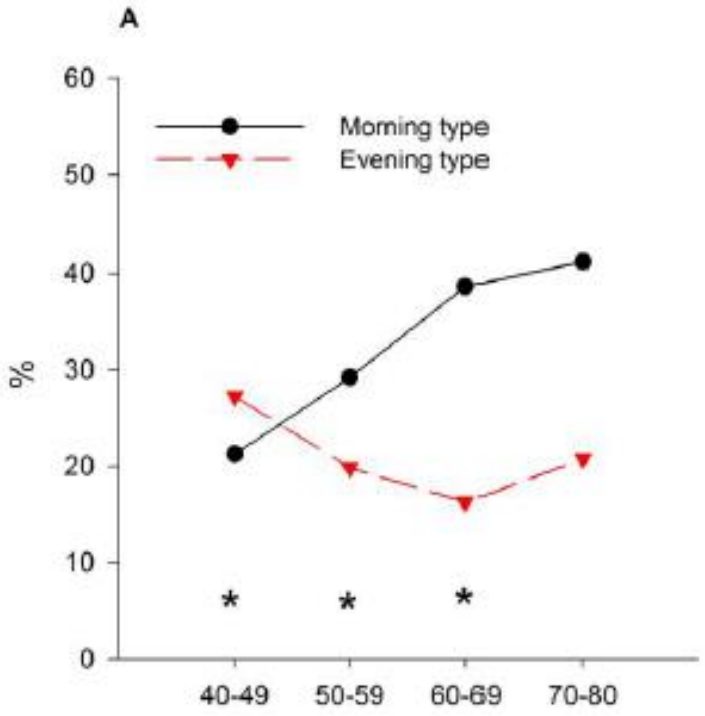
Subjects taking medication which interferes with sleep structure and/or duration (N=289), alcohol consumption (2 glasses of wine (or equivalent) consumed 4 hours prior to sleep recording (N=45), 4% oxygen desaturation index and AHI>15/h (N=366), and periodic limb movements index >15/hour(N=619): **1147 participants.**

Out of 1147 PSG recordings of normal sleepers, **776** which contained at least 4 sleep cycles and sleep efficiency > 80% were subjected to spectral analysis

Ann Med. 2015;47(6):482-91

Chronotype

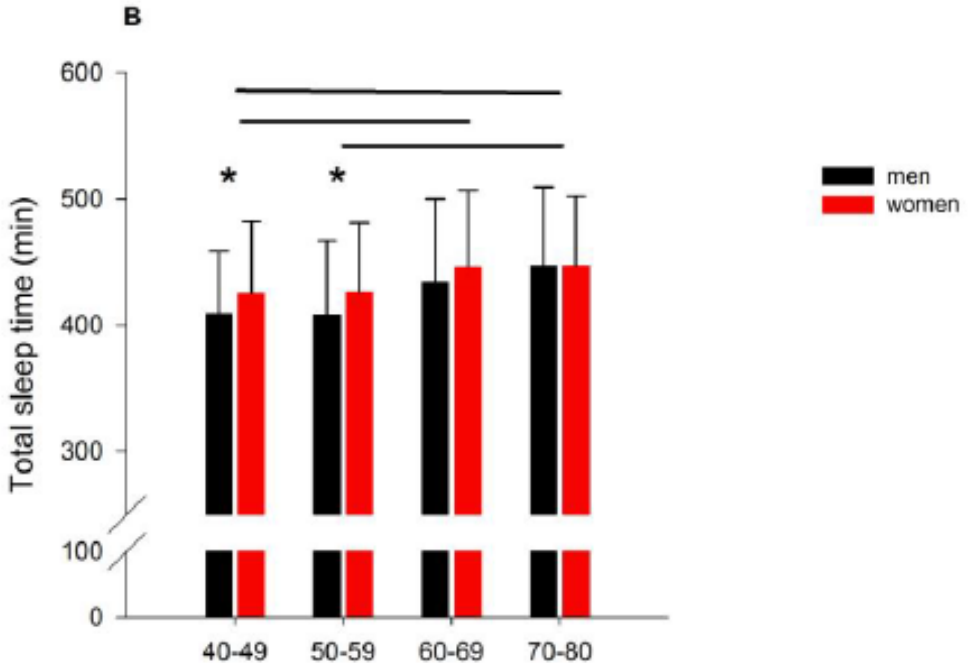
- Aging was associated with a gradual shift towards morningness.
- The likelihood of being morning type was 5.9 times higher in older subjects compared with younger ones



Ann Med. 2015;47(6):482-91

Chronotype

- Older subjects went to bed and fell asleep earlier than younger ones, and their subjective sleep duration was longer
- Gender effect was stronger for younger subjects, with women going to bed and falling asleep earlier, and sleeping longer



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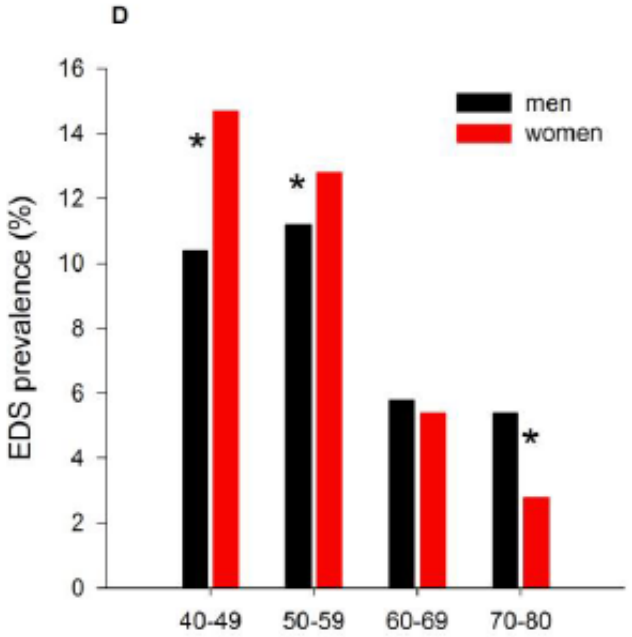
Daytime sleepiness

- The ESS score decreased with aging, and the reduction was larger in women
- The prevalence of excessive daytime sleepiness decreased with aging from 11.7% among participants aged 40-49 years to 6.4% in men and from 14.1 to 2.3% in women aged over 70



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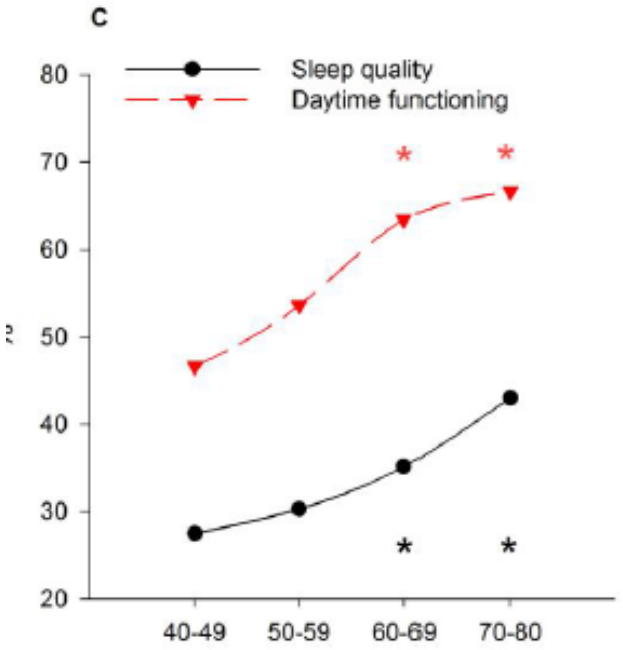
Subjective sleep quality

- Self-reported sleep quality and daytime functioning measured by PSQI improved with aging



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Polysomnographic data

- Sleep onset latency was not significantly affected by age or gender
- Sleep duration diminished by 28 minutes across age groups
- Sleep efficiency decreased with age
- SWS amount decreased with age
- Women slept 26 min longer than men
- Men, independent of age, had less SWS and REM sleep

	40-50 y.o.		50-60 y.o.		60-70 y.o.		70-80y.o.	
	women	men	women	men	women	men	women	men
Total sleep time (min) (1,2)	428.6 ± 60.7 [420.6-436.6]	398.5 ± 67.4 [389.5-407.3]	421.7 ± 63.7 [413.5-429.8]	388.4 ± 66.7 [377.9-398.8]	406.5 ± 67.5 [395.1-418.0]	381.4 ± 80.5 [363.3-399.4]	390.5 ± 72.0 [368.8-412.1]	379.6 ± 62.4 [358.5-400.7]
Sleep efficiency (%) (1,2)	90.4 ± 6.1 [89.6-91.2]	88.5 ± 8.3 [87.4-89.5]	88.7 ± 7.6 [87.7-89.6]	86.9 ± 8.9 [85.3-88.3]	83.0 ± 10.3 [81.2-84.7]	78.3 ± 12.4 [75.5-81.1]	78.7 ± 12.8 [74.8-82.5]	77.6 ± 11.7 [73.6-81.5]
Wake after sleep onset (min) (1,2)	46.3± 32.2 [42.1-50.6]	52.9± 40.1 [47.6-58.2]	54.8 ± 38.8 [49.9-59.8]	59.9 ± 43.4 [53.1-66.7]	85.8 ± 56.4 [76.2-95.4]	105.9 ± 63.9 [91.5-120.2]	107.8 ± 70.0 [86.8-128.9]	114.5 ± 74.7 [89.2-140.0]
Sleep onset latency (to any stage)(min)	15.0 ± 19.2 [12.5-17.6]	13.8 ± 16.0 [11.6-15.9]	16.5 ± 22.7 [13.6-19.4]	13.6 ± 14.1 [11.4-15.8]	19.0 ± 25.2 [14.7-23.3]	17.2 ± 20.1 [12.7-21.7]	18.8 ± 16.6 [13.8-23.8]	14.8 ± 15.6 [9.5-20.0]

Ann Med. 2015;47(6):482-91

Conclusions

- Age-related changes in sleep do not affect subjective sleepiness or daytime quality

- Presence of sleep complaints should not be viewed as part of normal aging, but should prompt the identification of underlying comorbidities

Ann Med. 2015;47(6):482-91

Association of socioeconomic status with sleep disturbances in the Swiss population-based CoLaus study

Silvia Stringhini [a,*], José Haba-Rubio [b], Pedro Marques-Vidal [a,c], Gérard Waeber [c], Martin Preisig [d], Idris Guessous [a,e,f], Pascal Bovet [a], Peter Vollenweider [c], Mehdi Tafti [b,g], Raphael Heinzer [b]

Sleep Medicine ■■ (2015) ■■–■■

- To examine the association of socioeconomic status with subjective and objective sleep disturbances:
  - **Educational level**
    - "high" (tertiary education), "middle" (upper secondary education or post-secondary non-tertiary education, including vocational education), and "low" (lower secondary education or lower)
  - **Occupational position**
    - "high" (entrepreneurs, professionals, higher managers), "middle" (self-employed, lower managers, skilled clerks), and "low" (unskilled clerks, farmers, skilled manual workers, unskilled manual workers).

Sleep Med. 2015;16:469-76

Association of socioeconomic status with sleep disturbances in the Swiss population-based CoLaus study

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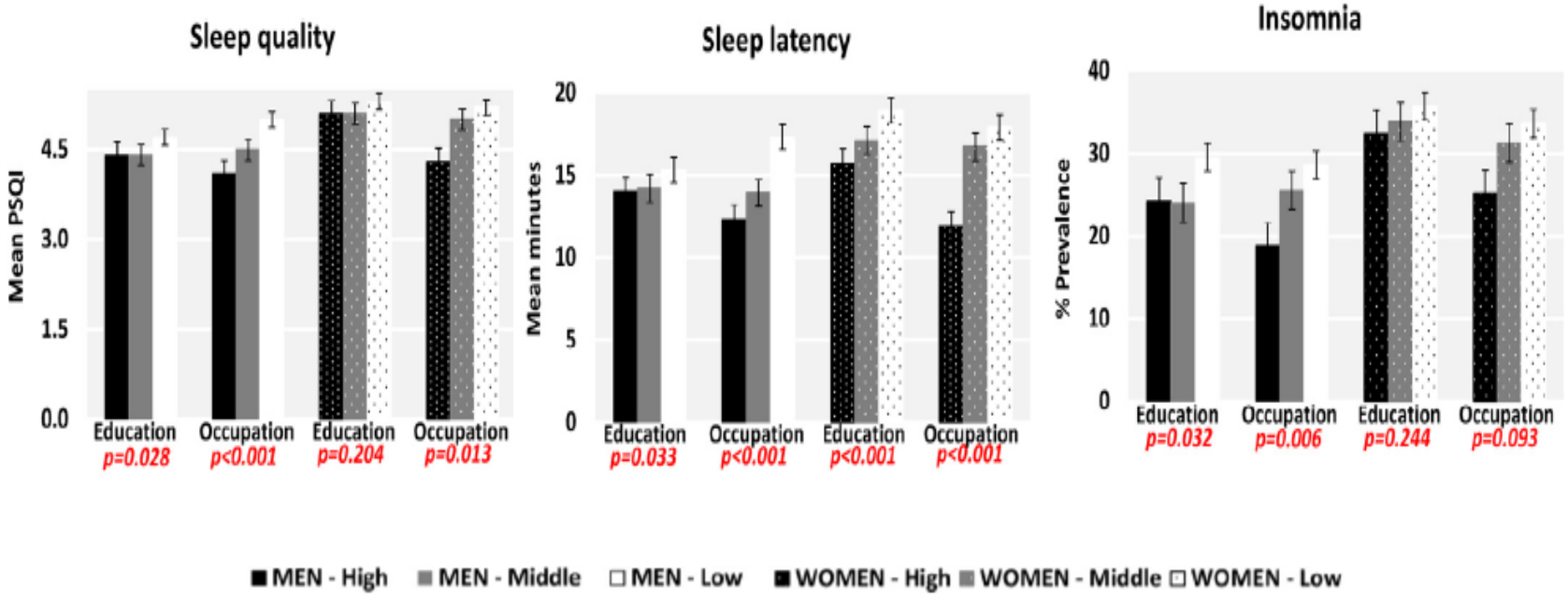
    - "high" (entrepreneurs, professionals, higher managers), "middle" (self-employed, lower managers, skilled clerks), and "low" (unskilled clerks, farmers, skilled manual workers, unskilled manual workers).

- The role of **socio-demographic**, **behavioural** and **psychological** factors in explaining this association

  - Socio-demographic factors
    - age, sex, employment status (employed full time/not), marital status (married or cohabiting/ living alone) and place of birth (Switzerland/other).
  - Behavioural factors
    - current smoking (yes vs no), heavy drinking (>21/>14 alcohol units/week in men/women vs lower amounts), sedentary behaviour [38] (lower tertile vs higher tertiles of total weekly energy expenditure I kcal/week, excluding energy expenditure during sleep), high coffee consumption (more than 6 cups/day), and obesity (body mass index >30 kg/m2)
  - Psychological factors
    - Depression, "somatic complaints," "depressed affect," "positive affect," and "interpersonal problems."

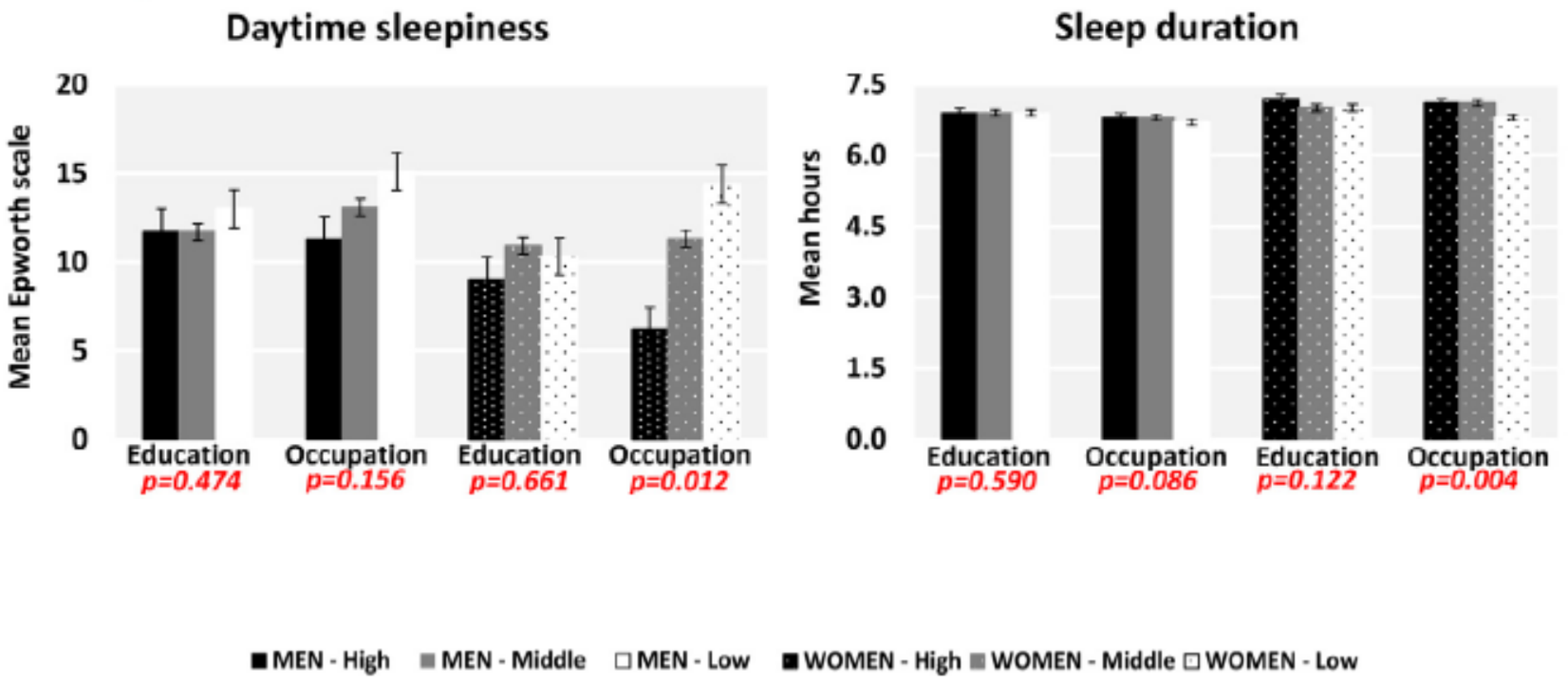
Sleep Med. 2015;16:469-76

- Men and women with a low educational level or low occupational position had poorer sleep quality, longer sleep latency, and higher prevalence of insomnia



Sleep Med. 2015;16:469-76

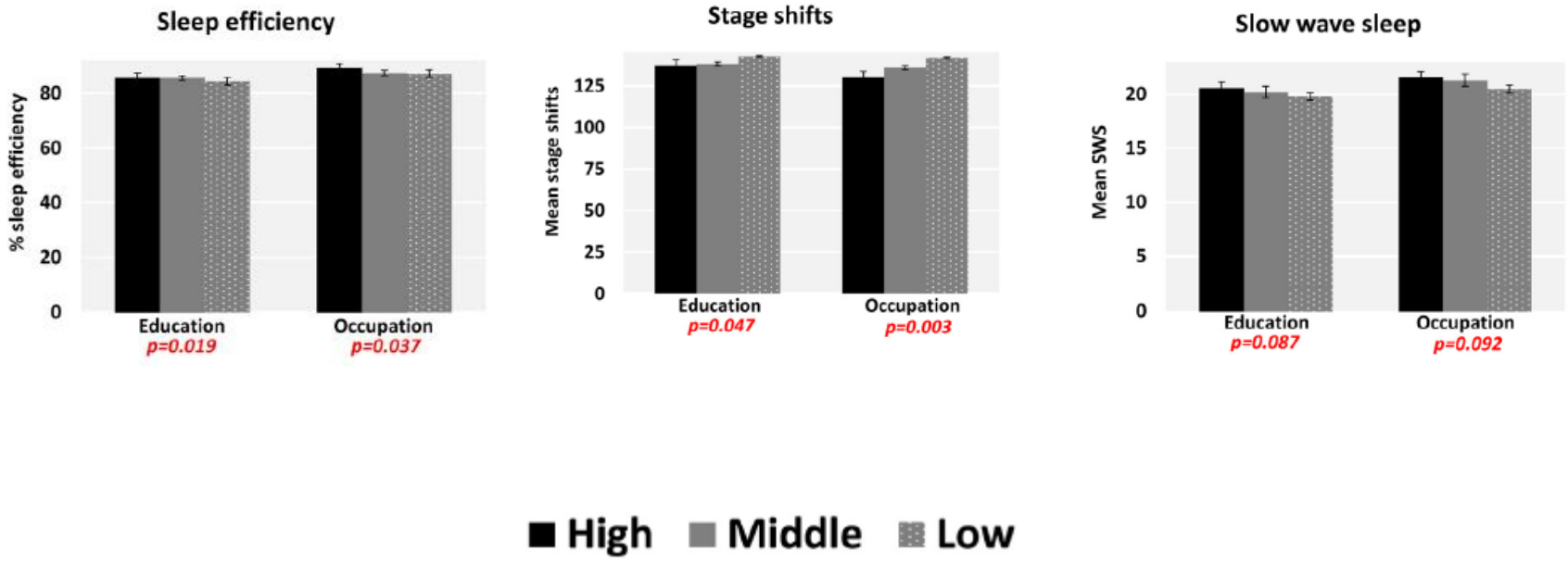
Women with a low (vs high) occupational position also had higher daytime sleepiness scores (Epworth mean score=14.4 vs 6.2, p<0.012) and a shorter sleep duration (mean hours=6.8 vs 7.1, p<0.004)



Sleep Med. 2015;16:469-76

Polysomnography

- Participants with low SES:
  - Lower sleep efficiency
  - Higher stage shifts
  - Decrease of deep sleep



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Socio-demographic, behavioural and psychological factors

- Psychological factors were strongly and consistently associated with most sleep disturbances in both sexes

- Depression, living alone and heavy drinking were associated with poor sleep quality

Sleep Med. 2015;16:469-76

Conclusions

- Sleep disturbances are frequent in the population but not equally distributed across socioeconomic strata, with people with a low SES sharing the highest burden

- The association of SES with sleep disturbances was particularly strong for occupational position

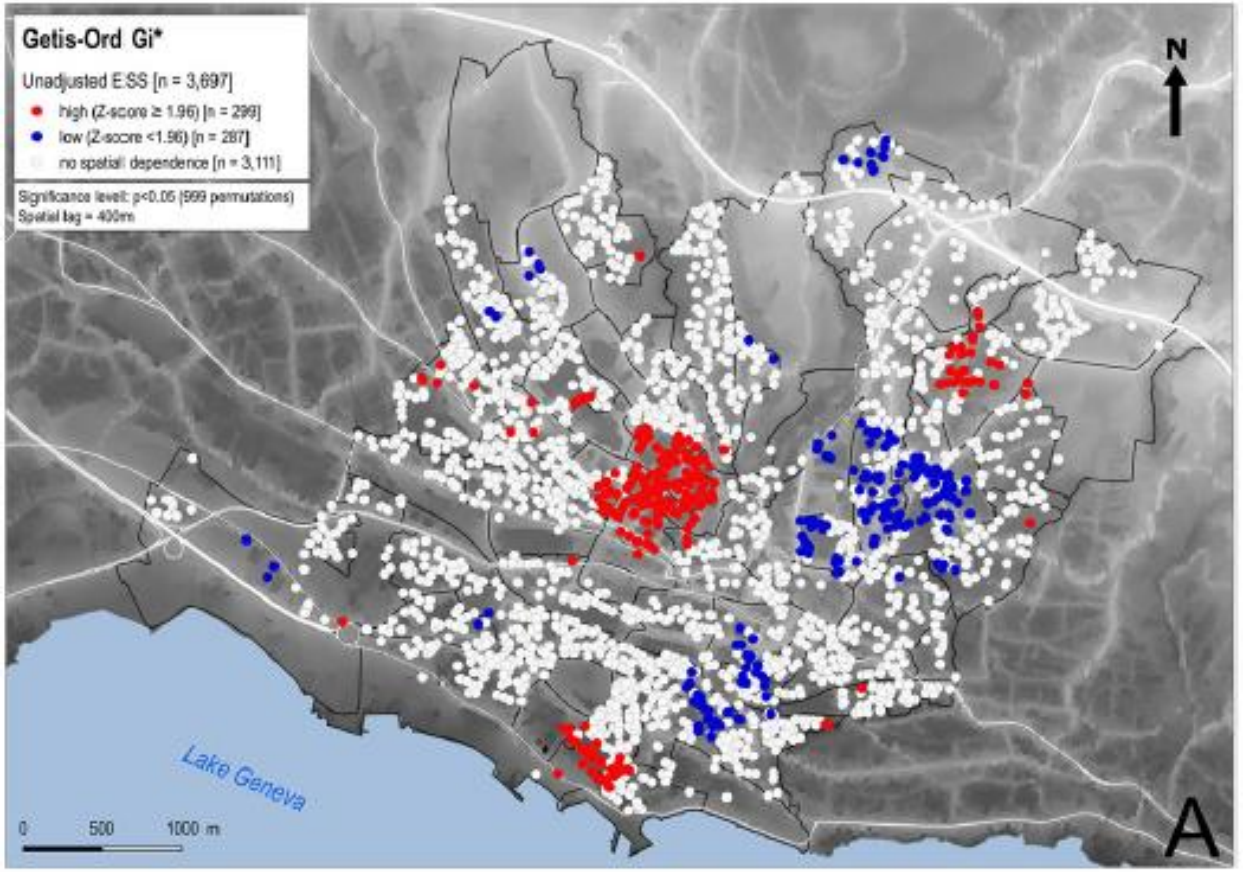
- Job characteristics (including workload, shift-work, and work-family demands) and psychological and financial stress

Sleep Med. 2015;16:469-76

Spatial clusters of daytime sleepiness and association with nighttime noise levels in a Swiss general population (GeoHypnoLaus)

Stéphane Joost[a,b,c,1], José Haba-Rubio[d,1], Rebecca Himsl[a,b,c], Peter Vollenweider[e], Martin Preisig[g], Gérard Waeber[e], Pedro Marques-Vidal[c,e], Raphaël Heinzer[d,2], Idris Guessous[b,c,f,2,*]

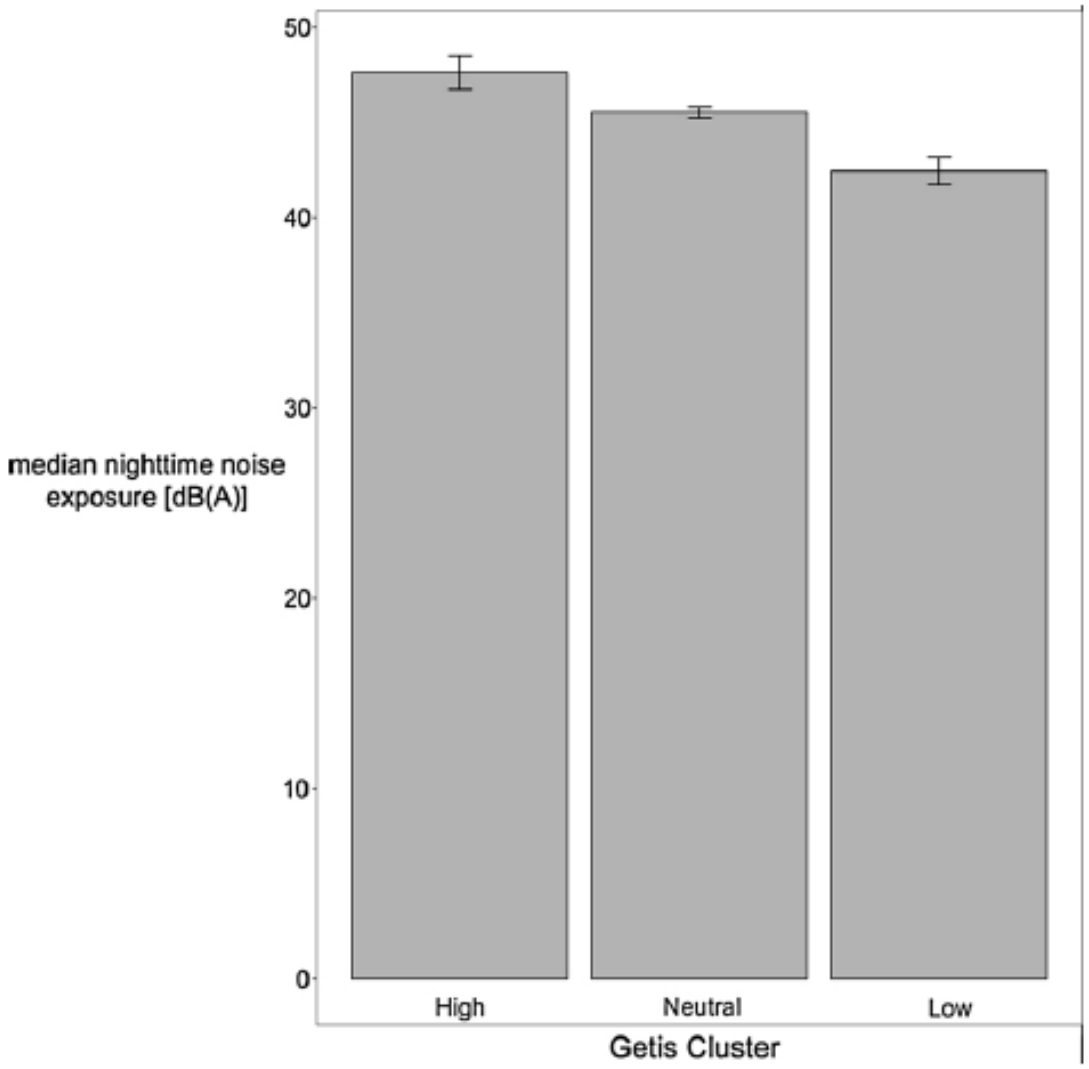
Daytime sleepiness is not randomly distributed and shows a significant spatial dependence



International Journal of Hygiene and Environmental Health 221 (2018) 951–957

The median nighttime traffic noise exposure was significantly different across the three ESS cluster classes (p <0.001).

The mean nighttime noise exposure in the high ESS cluster class was 47.6 db **5.2 dB higher** than in low clusters (p <0.001) and 2.1 dB higher than in the neutral class (p <0.001).



International Journal of Hygiene and Environmental Health 221 (2018) 951–957

Original Article

Bad sleep? Don't blame the moon! A population-based study

José Haba-Rubio [a], Pedro Marques-Vidal [b], Nadia Tobback [a], Daniela Andries [a], Martin Preisig [c], Christine Kuehner [d], Peter Vollenweider [b], Gérard Waeber [b], Gianina Luca [e], Mehdi Tafti [a,e], Raphaël Heinzer [a,f,*]

Table 1
Subjective sleep quality for full moon, waxing/waning moon, and new moon ($n = 1991$).

	Full moon ($n = 592$)	Waxing/waning moon ($n = 716$)	New moon ($n = 683$)	p value
Subjective quality				
Excellent	26 (4.4)	22 (3.1)	26 (3.8)	
Good	207 (35)	245 (34.2)	269 (39.4)	0.29
Average	284 (48)	352 (49.2)	313 (45.8)	
Bad	75 (12.7)	97 (13.6)	75 (11.0)	
Subjective quality				
Excellent + Good	233 (39.4)	267 (37.3)	295 (43.2)	0.08
Average + Bad	359 (60.6)	449 (62.7)	388 (56.8)	
Average + Bad *vs.* other	1 (ref.)	1.10 (0.87–1.38)	0.84 (0.67–1.06)	§

Results are expressed as number of participants and percentage. Statistical analysis by chi-squared or logistic regression (§) adjusting for gender, age, alcohol consumption (yes/no), sleep medicines (yes/no), and day of week.

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Sleep parameters for full moon, waxing/waning moon, and new moon ($n = 2125$).

	Full moon ($n = 641$)	Waxing/waning moon ($n = 755$)	New moon ($n = 729$)	p value
Total sleep time, min	398 ± 3	402 ± 3	403 ± 3	0.31
Latency to sleep, min	18.1 ± 0.9	16.5 ± 0.8	18.9 ± 0.9	0.13
Sleep efficiency, %	84.3 ± 0.4	84.4 ± 0.4	85.0 ± 0.4	0.31
No. of awakenings, nr	24.7 ± 0.5	25.5 ± 0.5	25.1 ± 0.5	0.53
Arousal index, nr/h	21.2 ± 0.4	21.5 ± 0.4	21.2 ± 0.4	0.82
No. of stage shifts, nr	138 ± 2	143 ± 2	141 ± 2	0.15
WASO, min	76.3 ± 2	76.5 ± 1.9	72.8 ± 1.9	0.32
REM latency, min	93.9 ± 2.4	94.8 ± 2.2	97.2 ± 2.3	0.59
Stage N1, min	46.5 ± 1	47.7 ± 0.9	46.4 ± 0.9	0.58
Stage N2, min	185 ± 2	188 ± 2	188 ± 2	0.39
Stage N2, %	46.2 ± 0.4	46.6 ± 0.4	46.5 ± 0.4	0.67
Stage N3, min	78.8 ± 1.3	76.8 ± 1.2	80 ± 1.2	0.14
Stage N3, %	19.9 ± 0.3	19.3 ± 0.3	19.9 ± 0.3	0.17
REM, min	87.9 ± 1.1	89.6 ± 1.0	88.6 ± 1.1	0.52
REM, %	21.9 ± 0.2	22.1 ± 0.2	21.7 ± 0.2	0.52
ODI3, nr/h	14.7 ± 0.6	14.8 ± 0.5	14.9 ± 0.5	0.95
AHI, nr/h	15.5 ± 0.6	15.5 ± 0.5	15.8 ± 0.5	0.91
PLMSI, nr/h	13.1 ± 0.9	13.9 ± 0.8	14.7 ± 0.8	0.41

WASO: Wake after sleep onset; REM: Rapid-eye-movement sleep; ODI3: Oxygen desaturation index ≥3%; AHI: Apnea/hypopnea index; PLMSI: Periodic leg movement index. Results are expressed as multivariable adjusted mean ± standard error. Statistical analysis by ANOVA, adjusting for gender, age, alcohol consumption (yes/no), sleep medicines (yes/no), and day of week.

Sleep Medicine 16 (2015) 1321–1326

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- Our study provides no scientific evidence for the widely popular belief that lunar phase and human sleep are related.

Sleep Medicine 16 (2015) 1321–1326

PREVALENCE OF SLEEP DISORDERS IN THE GENERAL POPULATION

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CENTRE DU SOMMEIL
DE FLORIMONT

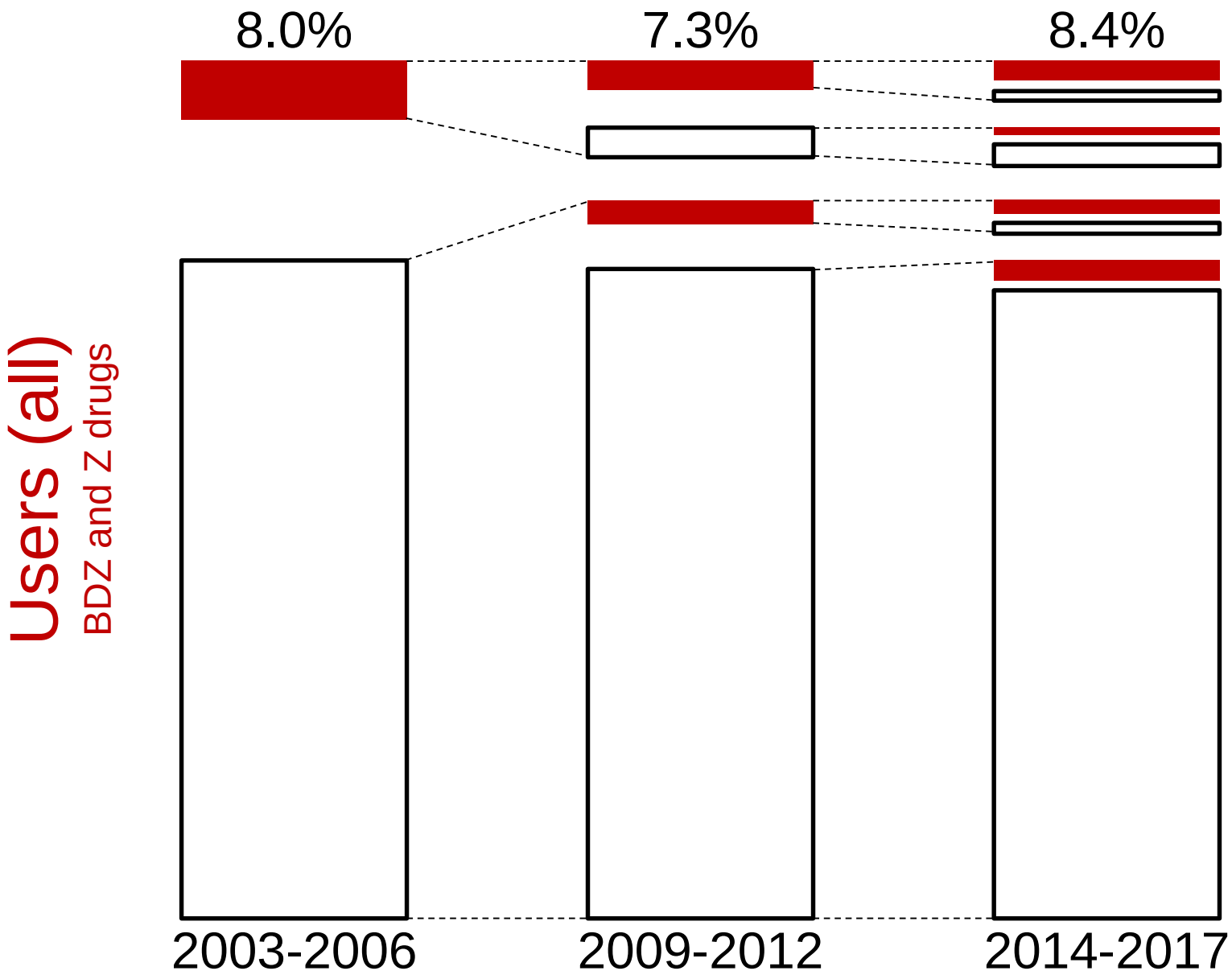
INSOMNIA

CoLaus/HypnoLaus

N= 5065 Women 52%; Age 57 years (40-81 years)

- **Sleep latency >30 minutes or nocturnal awakenings min 3 to 4 x / week**

Population:	32.7%	
Women:	36.3 %	
Men:	28.6 %	Sex diff: p<0.0001



HypnoLaus, unpublished data

Participants' characteristics according to presence/absence of sleeping pills

	Absent	Present	P-value
Sample size	2897	430	
Age (years)	56.3 ± 10.1	58.7 ± 10.3	<0.001
Men (%)	1436 (49.6)	137 (31.9)	<0.001
Body mass index (kg/m2)	25.8 ± 4.2	26.4 ± 4.9	0.008
Body mass index categories (%)			0.003
Normal	1360 (47.0)	182 (42.3)	
Overweight	1131 (39.0)	161 (37.4)	
Obese	406 (14.0)	87 (20.2)	
Living alone (%)	1145 (39.5)	220 (51.2)	<0.001
Sedentary (%)	1580 (54.5)	290 (67.4)	<0.001

Age, sex (women), overweight, sedentary, living alone

HypnoLaus, unpublished data

Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study

R Heinzer, S Vat, P Marques-Vidal, H Marti-Soler, D Andries, N Tobback, V Mooser, M Preisig, A Malhotra, G Waeber, P Vollenweider, M Tafti, J Haba-Rubio**

Lancet Respir Med 2015

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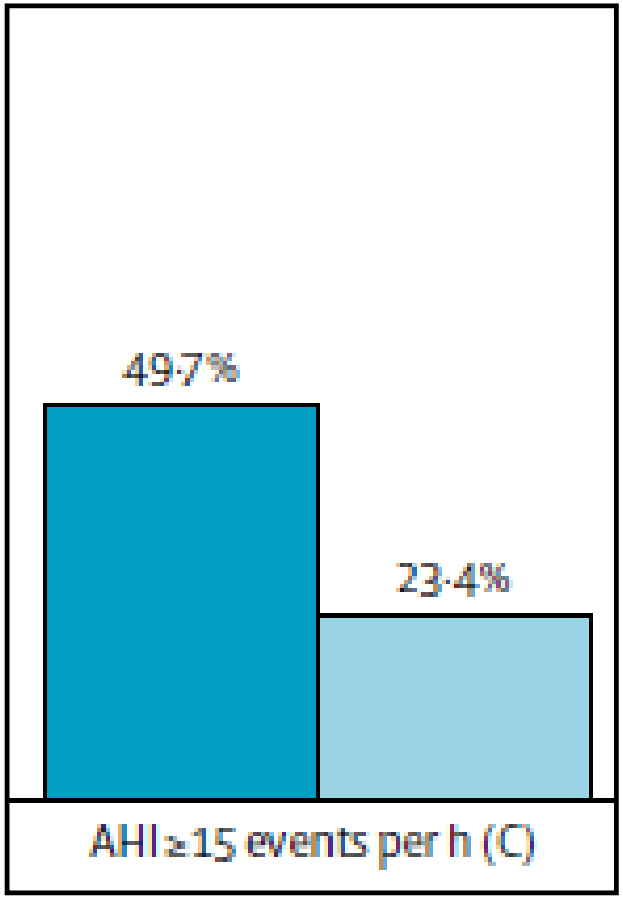

Lancet Respir Med 2015

Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study

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	Men				Women			
	Mild-to-severe	p value	Moderate-to-severe	p value	Mild-to-severe	p value	Moderate-to-severe	p value
Age (per 10-year increment)	1·32 (1·13–1·52)	0·0008	1·53 (1·38–1·68)	<0·0001	1·72 (1·53–1·90)	<0·0001	1·72 (1·50–1·94)	<0·0001
BMI (kg/m²)								
25–30 (*vs* <25)	1·82 (1·13–2·91)	0·0132	1·74 (1·16–2·59)	0·0058	3·25 (2·12–4·97)	<0·0001	1·90 (1·16–3·12)	0·0110
>30 (*vs* <25)	4·18 (1·50–11·7)	0·0062	2·84 (1·51–5·34)	0·0012	2·43 (1·23–4·82)	0·0110	1·75 (0·87–3·54)	0·1171
Neck circumference (per 1 cm increment)	1·02 (0·93–1·13)	0·6296	1·11 (1·03–1·20)	0·0044	1·07 (0·97–1·17)	0·1685	1·14 (1·03–1·26)	0·0135
Waist-to-hip ratio (per quartile increment)*								
Quartile 2 (*vs* quartile 1)	1·16 (0·72–1·86)	0·5376	1·35 (0·88–2·06)	0·4681	1·47 (0·93–2·32)	0·0951	1·27 (0·67–2·39)	0·4657
Quartile 3 (*vs* quartile 1)	1·54 (0·86–2·78)	0·1490	1·22 (0·77–1·93)	0·4017	1·72 (1·10–2·69)	0·0176	1·86 (1·04–3·34)	0·0376
Quartile 4 (*vs* quartile 1)	1·82 (0·94–3·50)	0·0738	1·47 (0·92–2·37)	0·1098	1·76 (1·02–3·04)	0·0406	1·85 (0·98–3·52)	0·0595

Lancet Respir Med 2015

Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study

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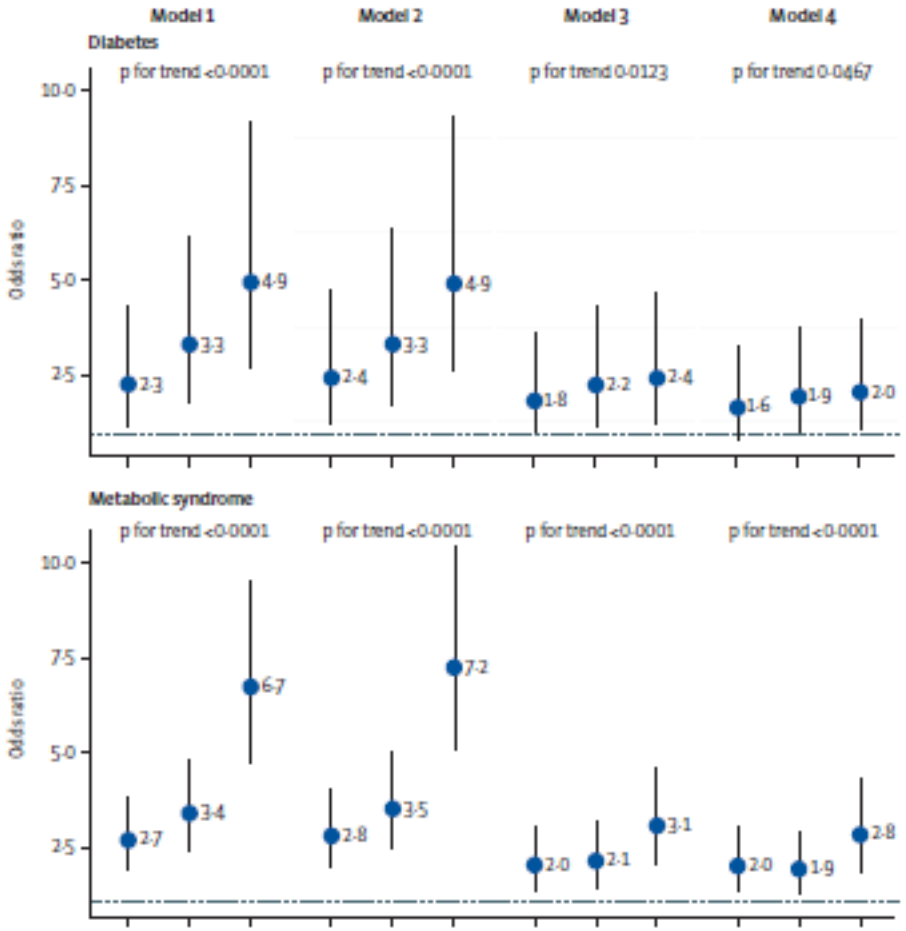
Diabetes

Metabolic syndrome



Lancet Respir Med 2015

Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study

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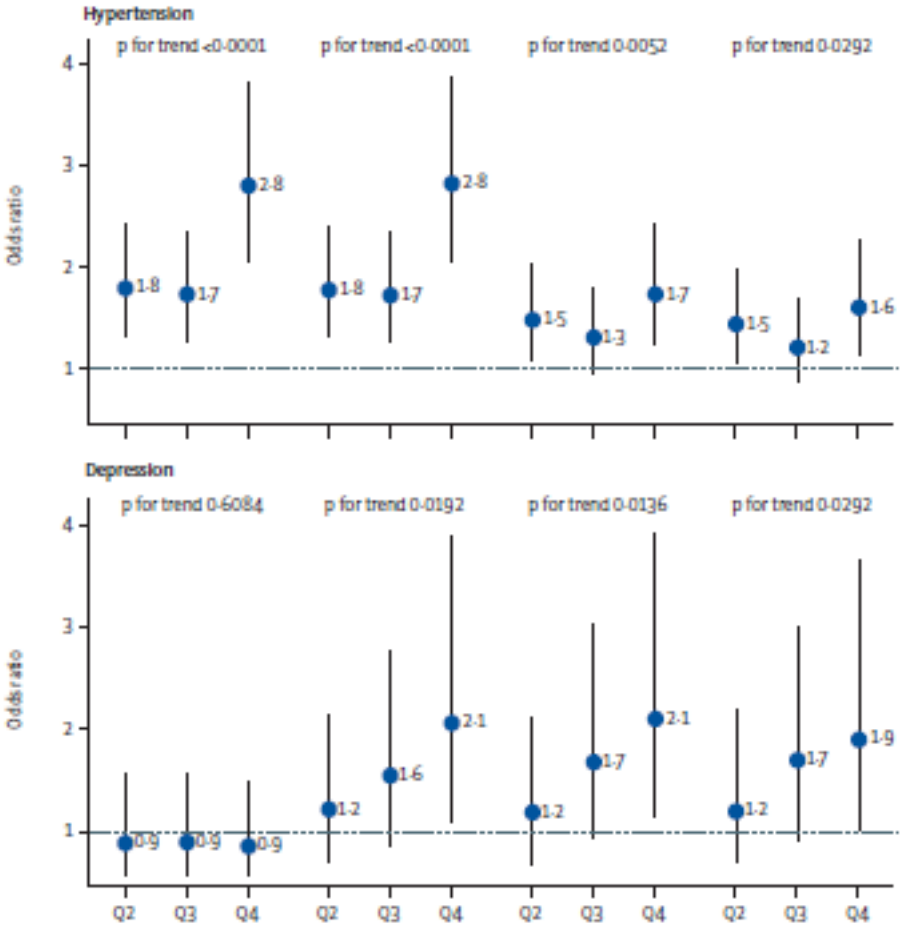
Hypertension

Diabetes



Lancet Respir Med 2015

Periodic limb movements

- A **PLMSI>15/h** is considered to be of potential clinical significance (according to the International Classification of Sleep Disorders, 3rd ed, 2014).

Annals of NEUROLOGY
An Official Journal of the American Neurological Association and the Child Neurology Society

Prevalence and Determinants of Periodic Limb Movements in the General Population

José Haba-Rubio, MD,[1] Helena Marti-Soler, PhD,[2] Pedro Marques-Vidal, MD, PhD,[3] Nadia Tobback, RPSGT,[1] Daniela Andries, RPSGT,[1] Martin Preisig, MD,[4] Gérard Waeber, MD,[3] Peter Vollenweider, MD,[3] Zoltán Kutalik, PhD,[2,5] Mehdi Tafti, PhD,[1,6] and Raphaël Heinzer, MD, MPH[1,7]

- Prevalence of PLMSI>15/h:

>15/h

28.6%

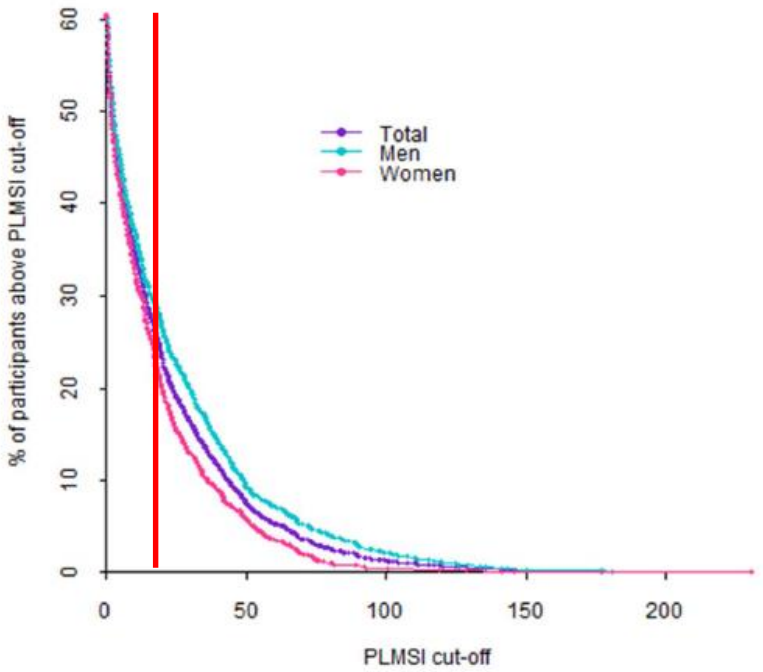


Figure 2: Prevalence of PLMSI throughout the entire range of potential cut-off values.
127x127mm (96 x 96 DPI)

J Haba-Rubio et al, **ANN NEUROL 2015**

Association between demographic, clinical and genetic features and PLMSI >15/h

	OR	(95% CI)	P value
Age (per one year increase)	**1.067**	**(1.053 - 1.082)**	<0.001
Gender (man)	**1.501**	**(1.143- 1.972)**	0.004
BMI (per one unit increase)	1.023	(0.989- 1.059)	0.180
Hypertension (yes vs. no)	1.145	(0.864- 1.517)	0.346
Diabetes (yes vs. no)	1.107	(0.737- 1.663)	0.625
Restless legs syndrome (yes vs. no)	**1.926**	**(1.405- 2.641)**	<0.001
AHI (log)	0.893	(0.787- 1.013)	0.079
Alcohol consumption (yes vs. no)	1.186	(0.824- 1.706)	0.359
Coffee consumption (reference: 0 cups)			
1-3 cups/day	1.331	(0.751- 2.359)	0.328
4-6 cups/day	1.160	(0.630- 2.137)	0.634
6+ cups/day	1.853	(0.782- 4.390)	0.161
Tobacco consumption (yes vs. no)	1.111	(0.802- 1.538)	0.526
Antidepressant intake (yes vs. no)	**1.519**	**(1.004- 2.297)**	0.048
Ferritin level	0.905	(0.759- 1.080)	0.273
rs3923809 allele (reference: GG)			
AG	**1.944**	**(1.162- 3.252)**	<0.001
AA	**3.513**	**(2.122- 5.815)**	<0.001

J Haba-Rubio et al, ANN NEUROL 2015

Conclusion :

- PLMS are highly prevalent in the general population

- Age, male gender, RLS, antidepressant intake and specific genetic polymorphisms are independent predictors of a PLMSI higher than 15/h

Clinical significance of periodic limb movements during sleep: the HypnoLaus study

José Haba-Rubio [a, *], Helena Marti-Soler [b], Nadia Tobback [a], Daniela Andries [a], Pedro Marques-Vidal [c], Peter Vollenweider [c], Martin Preisig [d], Raphael Heinzer [a]

- PLMS are associated with objective sleep disturbances
- PLMS "per se" do not seem to be an independent cardiometabolic risk factor

Sleep Medicine 41 (2018) 45–50

PREVALENCE OF REM SLEEP BEHAVIOR DISORDER

UNIL | Université de Lausanne
Faculté de médecine
Rue du Bugnon 7
CH-1011 Lausanne

CHUV

CENTRE DU SOMMEIL
DE FLORIMONT

REM sleep behavior disorder

- REM sleep behavior disorder (RBD) is a parasomnia characterized by unpleasant dreams, motor behaviors in which the patients seem to be enacting their dreams and a loss of normal muscle atonia in REM sleep during PSG
- Follow-up of patients with RBD shows that a significant number of them will develop a neurodegenerative disorder (Iranzo A et al, Lancet Neurol 2013)

Prevalence and determinants of rapid eye movement sleep behavior disorder in the general population

José Haba-Rubio[1*], Birgit Frauscher[2], Pedro Marques-Vidal[3], Jérôme Toriel[1], Nadia Tobback[1], Daniela Andries[1], Martin Preisig[4], Peter Vollenweider[3], Ronald Postuma[5], and Raphaël Heinzer[1,6]

Sleep Research Society®

1) Munich Parasomnia Screening (*S Fulda et al*, Somnologie 2008)

- Two questions regarding possible RBD
  - "Have you ever lashed about, hitting or kicking? **AND**
  - "Have you ever actually done what you dreamt, e.g. gesticulating or lashing about?"

2) Loss of physiological muscle atonia in REM

Prevalence of 1.06% (95% CI=0.61-1.50) of RBD in the general population

no difference between men and women

Sleep, 2018

SLEEP AND COGNITION

UNIL | Université de Lausanne
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CHUV

CENTRE DU SOMMEIL
DE FLORIMONT

Introduction

- Sleep disturbances are particularly frequent in individuals with cognitive deficits such as mild cognitive impairment (MCI) and dementia

Sleep and Alzheimer's disease

Laure Peter-Derex [a,b,c,*], Pierre Yammine [d], Hélène Bastuji [b,c,e], Bernard Croisile [f]

- 45% of patients with AD
- Sleep disorders in patients with AD are qualitatively similar to those seen in normal elderly, but much more severe

- Alteration of sleep architecture:
  - Increase:
    - Wake after sleep onset
    - Sleep latency
  - Decrease
    - Total sleep time
    - Slow wave sleep
    - REM sleep (which is relatively preserved during normal aging: cholinergic dysfunction)

Sleep Medicine Reviews 19 (2015) 29–38

Sleep is related to neuron numbers in the ventrolateral preoptic/intermediate nucleus in older adults with and without Alzheimer's disease

BRAIN
A JOURNAL OF NEUROLOGY

Andrew S. P. Lim,[1,2,3] Brian A. Ellison,[2,3] Joshua L. Wang,[2,3] Lei Yu,[4] Julie A. Schneider,[4] Aron S. Buchman,[4] David A. Bennett[4] and Clifford B. Saper[2,3]

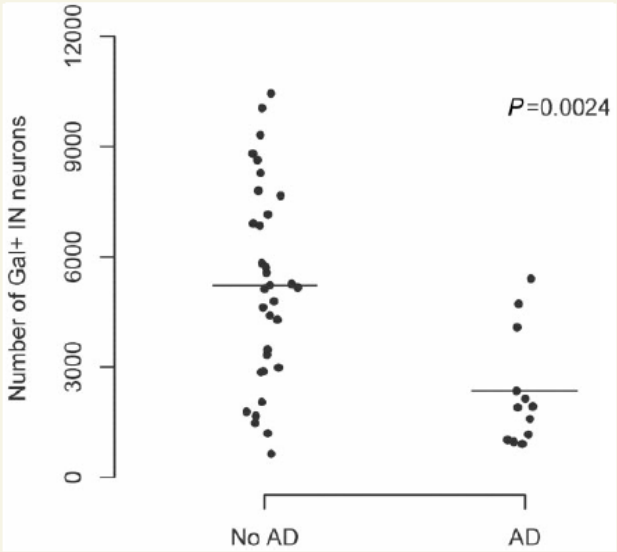
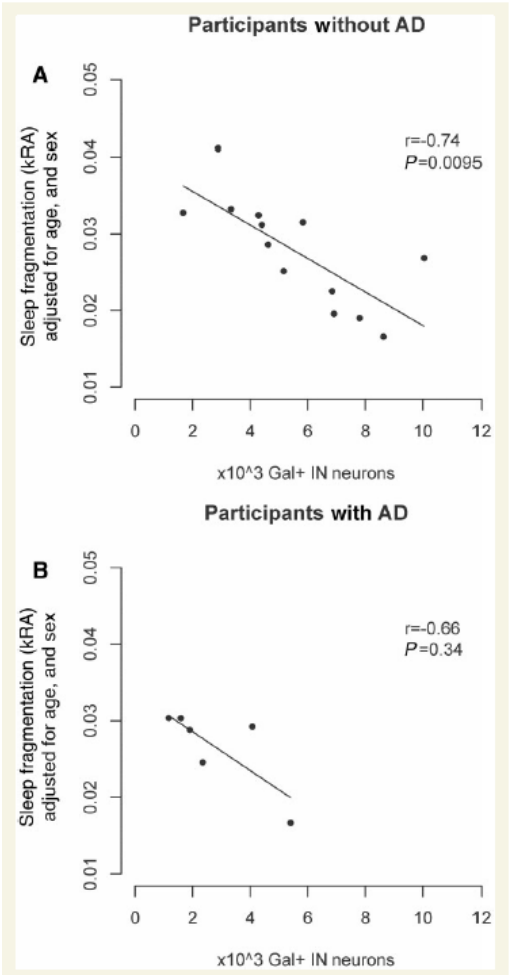


Figure 2 The presence of Alzheimer's disease (AD) is associated with fewer galanin-immunoreactive neurons in the intermediate nucleus (IN) (n = 45).



Sleep and Alzheimer's disease

Laure Peter-Derex [a,b,c,*], Pierre Yammine [d], Hélène Bastuji [b,c,e], Bernard Croisile [f]

- Degeneration of pathways that regulate wake/sleep and sleep architecture, as well as somatic or psychiatric comorbidities

- Sleep disorders can exacerbate cognitive symptoms by altering sleep-dependent memory consolidation processes

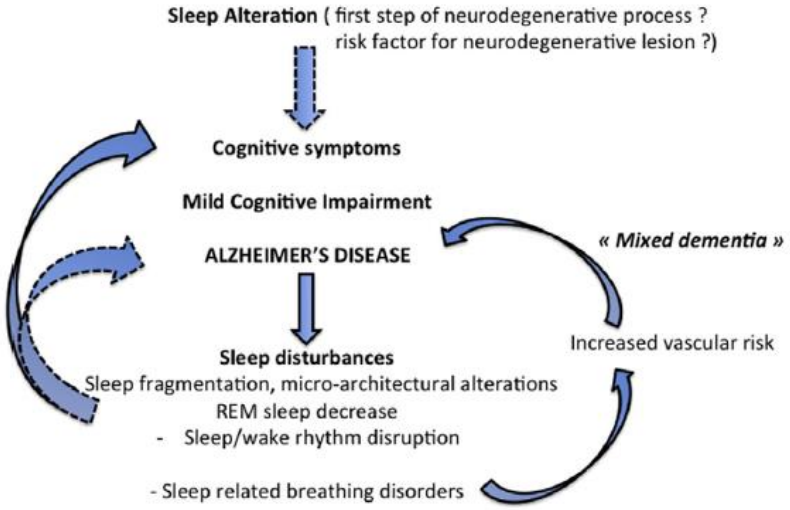


Fig. 1. Possible interactions between sleep disorders and Alzheimer's disease.

Sleep Medicine Reviews 19 (2015) 29–38

Introduction

- Sleep is a vital biological function, essential for brain restoration and memory consolidation

- Accumulating evidence suggests that sleep duration can play a role in the pathogenic process leading to cognitive impairment

Sleep Quality and 1-Year Incident Cognitive Impairment in Community-Dwelling Older Adults

Olivier Potvin, PhD[1,2,3]; Dominique Lorrain, PhD[1,4]; Hélène Forget, PhD[5]; Micheline Dubé, PhD[6]; Sébastien Grenier, PhD[7]; Michel Préville, PhD[1,2]; Carol Hudon, PhD[3,8]

Table 3—Subjective sleep duration and incident cognitive impairment in older men and women (n = 1,664)

	Incident Cognitive Impairment								
			General			Amnestic		Nonamnestic	
Sleep Duration	Yes n (%)	No n (%)	Crude OR (95% CI)	Adjusted* OR (95% CI)	P	Adjusted* OR (95% CI)	P	Adjusted* OR (95% CI)	P
Women	**n = 68**	**n = 1091**							
Long (≥ 9 hr)	14 (20.6)	136 (12.5)	1.97 (1.05-3.70)	2.10 (1.10-4.00)	0.024	3.70 (1.49-9.17)	0.005	1.34 (0.54-3.34)	0.530
Short (≤ 5 hr)	11 (16.2)	131 (12.0)	1.61 (0.81-3.20)	1.31 (0.65-2.65)	0.454	1.60 (0.56-4.61)	0.382	1.18 (0.47-2.95)	0.729
Average (> 5 hr and < 9 hr)	43 (63.2)	824 (75.5)	Ref	Ref		Ref		Ref	
Men	**n = 37**	**n = 468**							
Long (≥ 9 hr)	1 (2.7)	50 (10.7)	0.29 (0.04-2.16)	0.26 (0.03-2.03)	0.200	0.51 (0.06-4.26)	0.533	-	-
Short (≤ 5 hr)	10 (27.0)	46 (9.8)	3.11 (1.41-6.86)	2.91 (1.24-6.82)	0.014	4.95 (1.72-14.27)	0.003	1.19 (0.25-5.64)	0.830
Average (> 5 hr and < 9 hr)	26 (70.3)	372 (79.5)	Ref	Ref		Ref		Ref	

CI, confidence interval; OR, odds ratio; Ref, reference category. *OR and 95% CI were estimated by a logistic regression with incident cognitive impairment as the predicted variable adjusted for age, education, Mini-Mental State Examination score at baseline, depressive episodes, anxiety, psychotropic drug use, cardiovascular conditions, and chronic diseases. P values were obtained by Wald *F* statistics with *df* = 1.

SLEEP 2012;35(4):491-499.

Sleep duration, cognitive decline, and dementia risk in older women

Jiu-Chiuan Chen[a,*], Mark A. Espeland[b], Robert L. Brunner[c], Laura C. Lovato[b], Robert B. Wallace[d], Xiaoyan Leng[b], Lawrence S. Phillips[e], Jennifer G. Robinson[d], Jane M. Kotchen[f], Karen C. Johnson[g], JoAnn E. Manson[h], Marcia L. Stefanick[i], Gloria E. Sarto[j], W. Jerry Mysiw[k]

Table 2
Incidence rates for having significant cognitive decline and MCI/dementia by sleep duration in WHIMS cohort, 1995–2008

	Hours of sleep per night				
≥8 points decrease in 3MS	≤5	6	7	8	≥9
N	664	2078	2615	1562	286
Total person-years at risk	4549.26	15,254.74	19,776.87	11,548.77	2036.58
Number of significant cognitive decline	88	269	246	169	30
Event rate (cases per 1000 person-years)*	19.34	17.63	12.44	14.63	14.73
	Hours of sleep per night				
MCI/dementia	≤5	6	7	8	≥9
N	693	2149	2686	1610	298
Total person-years at risk	4902.59	16,352.33	21,158.47	12,387.62	2182.33
Number of MCI/dementia	65	188	163	110	23
Event rate (cases per 1000 person-years)*	13.26	11.50	7.70	8.88	10.54

Alzheimer's & Dementia 12 (2016) 21-33

Self-reported sleep duration and cognitive functioning in the general population

ERKKI KRONHOLM[1], MIKAEL SALLINEN[2,3], TIMO SUUTAMA[4], RAIMO SULKAVA[5], PERTTI ERA[6] and TIMO PARTONEN[7]

Table 2 Sleep factors as explanatory variables (in generalized logistic regression models) of subjective memory function in the adult general population (type 3 analysis of effects are shown)

		Model I		*Model II*		*Model III*	
		$n = 5171$; $r^2 = 0.1019$		$n = 5171$; $r^2 = 0.2900$		$n = 5171$; $r^2 = 0.3008$	
Sleep factor	*df*	*Wald* χ^2	P	*Wald* χ^2	P	*Wald* χ^2	P
Fatigue and tiredness	4	107.1	<0.0001	66.8	<0.0001	46.0	<0.0001
Exceptional tiredness	4	49.1	<0.0001	47.5	<0.0001	42.0	<0.0001
Sleep duration	6	42.6	<0.0001	18.5	0.005	12.4	0.054
Insomnia or sleep disorder	4	28.2	<0.0001	14.7	0.005	10.9	0.028
Use of hypnotics	2	16.3	0.0003	0.6	0.723	0.5	0.768
Probable sleep apnoea	2	12.1	0.002	1.5	0.474	0.9	0.629

Model I is the best (in terms of r^2) model including only sleep factors as explanatory variables. Model II is adjusted for the sociodemographic factors (gender, age and education). Model III is adjusted for the sociodemographic factors + health factors (depression, alcohol dependency, use of neuroleptics, use of antidepressants and 11 diseases).

J. Sleep Res. (2009) 18, 436–446

Measures of Sleep–Wake Patterns and Risk of Mild Cognitive Impairment or Dementia in Older Women

Susan J. Diem, M.D., M.P.H., Terri L. Blackwell, M.A., Katie L. Stone, Ph.D., Kristine Yaffe, M.D., Greg Tranah, Ph.D., Jane A. Cauley, Dr.P.H., Sonia Ancoli-Israel, Ph.D., Susan Redline, M.D., M.P.H., Adam P. Spira, Ph.D., Teresa A. Hillier, M.D., M.S., Kristine E. Ensrud, M.D., M.P.H.

TABLE 3. Variability in Objective Sleep Measures and Odds of MCI or Dementia

Predictor (SD over all nights)	Outcome = MCI or Dementia vs. Normal			
	Minimally Adjusted[a]		Multivariate Adjusted[b]	
	OR (95% CI)	Wald χ^2 [1, N = 1,343], p	OR (95% CI)	Wald χ^2 [1, N = 1,330], p
Total sleep time, min				
Q1 (<28.58)	1.00 (reference)	—	1.00 (reference)	—
Q2 (28.58 to <42.16)	0.81 (0.58–1.14)	1.49, p = 0.22	0.82 (0.58–1.17)	1.21, p = 0.27
Q3 (42.16 to <61.04)	0.96 (0.68–1.34)	0.07, p = 0.79	0.98 (0.69–1.38)	0.02, p = 0.89
Q4 (≥61.04)	1.36 (0.97–1.91)	3.26, p = 0.07	1.40 (0.98–1.98)	3.47, p = 0.06
p Trend		4.02, p = 0.045		4.05, p = 0.04
Sleep efficiency, %				
Q1 (<2.99)	1.00 (reference)	—	1.00 (reference)	—
Q2 (2.99 to <4.93)	1.83 (1.30–2.57)	12.00, p = 0.0005	1.89 (1.33–2.69)	12.50, p = 0.0004
Q3 (4.93 to <7.92)	1.43 (1.01–2.02)	4.11, p = 0.04	1.48 (1.04–2.12)	4.60, p = 0.03
Q4 (≥7.92)	1.87 (1.32–2.64)	12.65, p = 0.0004	1.92 (1.34–2.75)	12.74, p = 0.0004
p Trend		8.40, p = 0.004		8.66, p = 0.003
WASO, min				
Q1 (<11.64)	1.00 (reference)	—	1.00 (reference)	—
Q2 (11.64 to <20.33)	1.31 (0.94–1.83)	2.52, p = 0.11	1.29 (0.91–1.82)	2.10, p = 0.15
Q3 (20.33 to <37.44)	1.21 (0.86–1.69)	1.17, p = 0.28	1.22 (0.86–1.73)	1.26, p = 0.26
Q4 (≥37.44)	1.24 (0.88–1.75)	1.54, p = 0.21	1.25 (0.87–1.78)	1.48, p = 0.22
p Trend		1.04, p = 0.31		1.11, p = 0.29
Sleep latency, min				
Q1 (<10.10)	1.00 (reference)	—	1.00 (reference)	—
Q2 (10.10 to <18.15)	1.00 (0.71–1.40)	0.00, p = 1.00	0.98 (0.69–1.38)	0.02, p = 0.90
Q3 (18.15 to <33.89)	0.94 (0.67–1.32)	0.11, p = 0.74	0.92 (0.65–1.31)	0.20, p = 0.66
Q4 (≥33.89)	1.36 (0.98–1.91)	3.30, p = 0.07	1.37 (0.97–1.94)	3.20, p = 0.07
p Trend		2.66, p = 0.10		2.60, p = 0.11

Notes: A separate model was run for each predictor.
[a]Adjusted for age, race, clinic, and education.
[b]Adjusted for age, race, clinic, education, body mass index, number of depressive symptoms, comorbidities, number of IADL impairments, smoking status, alcohol use, exercise, living alone, self-reported health status, antidepressant use, benzodiazepine use, and prescription sleep medication use.

Am J Geriatr Psychiatry 24:3, March 2016

Self-reported Sleep and β-Amyloid Deposition in Community-Dwelling Older Adults

Adam P. Spira, PhD; Alyssa A. Gamaldo, PhD; Yang An, MS; Mark N. Wu, MD, PhD; Eleanor M. Simonsick, PhD; Murat Bilgel, BS; Yun Zhou, PhD; Dean F. Wong, MD, PhD; Luigi Ferrucci, MD, PhD; Susan M. Resnick, PhD

Table 3. Association Between Sleep Variables and cDVRs[a]

	Unadjusted			Multivariable Adjusted[b]		
	B Value (95% CI)	Correlation Coefficient, *r*	*P* Value[c]	B Value (95% CI)	Partial Correlation Coefficient, *r*[d]	*P* Value[c]
Shorter sleep duration						
cDVR	0.06 (0.004 to 0.11)	0.27	.04	0.08 (0.03 to 0.14)	0.38	.005
Precuneus DVR	0.07 (0.0001 to 0.14)	0.25	.05	0.11 (0.03 to 0.18)	0.36	.007
Trouble falling asleep[e]						
cDVR	0.04 (−0.002 to 0.07)	0.22	.07	0.03 (−0.003 to 0.07)	0.23	.07
Precuneus DVR	0.04 (−0.007 to 0.10)	0.20	.09	0.05 (−0.01 to 0.10)	0.23	.08
Wake several times[e]						
cDVR	0.01 (−0.02 to 0.04)	0.08	.49	0.01 (−0.02 to 0.04)	0.05	.72
Precuneus DVR	0.01 (−0.03 to 0.05)	0.07	.56	0.01 (−0.03 to 0.05)	0.05	.69
Worse sleep quality[e]						
cDVR	0.06 (0.01 to 0.10)	0.28	.02	0.04 (−0.01 to 0.09)	0.19	.13
Precuneus DVR	0.09 (0.03 to 0.16)	0.34	.004	0.08 (0.01 to 0.15)	0.29	.03
WHIIRS total score						
cDVR	0.01 (−0.0001 to 0.02)	0.23	.052	0.01 (−0.004 to 0.02)	0.16	.23
Precuneus DVR	0.01 (−0.0002 to 0.03)	0.23	.054	0.01 (−0.004 to 0.02)	0.18	.16

JAMA Neurol. 2013;70(12):1537-1543.

Introduction

- Sleep is a vital biological function, essential for brain restoration and memory consolidation

- Accumulating evidence suggests that sleep duration, sleep fragmentation can play a role in the pathogenic process leading to cognitive impairment

Modification of the Relationship of the Apolipoprotein E ε4 Allele to the Risk of Alzheimer Disease and Neurofibrillary Tangle Density by Sleep

Andrew S. P. Lim, MD; Lei Yu, PhD; Matthew Kowgier, PhD; Julie A. Schneider, MD; Aron S. Buchman, MD; David A. Bennett, MD

Table 2. Effect of Degree of Sleep Consolidation and Presence/Absence of the *APOE* ε4 Allele on the Risk of Incident AD

	Effect on Risk of Incident AD[a]			
Predictor	Model A	Model B	Model C	Model D
Sleep consolidation	0.84 (0.71-1.00)		0.84 (0.71-0.99)	0.83 (0.63-1.10)
P value	.05		.04	.19
APOE genotype		2.21 (1.44-3.40)	2.22 (1.44-3.42)	2.70 (1.51-4.83)
P value		.001	.001	.001
Sleep consolidation × *APOE* genotype				0.67 (0.46-0.97)
P value				.04

JAMA Neurol. 2013;70(12):1544-1551.

Sleep Quality and Preclinical Alzheimer Disease

Yo-El S. Ju, MD; Jennifer S. McLeland, MSW, MA; Cristina D. Toedebusch, BS; Chengjie Xiong, PhD; Anne M. Fagan, PhD; Stephen P. Duntley, MD; John C. Morris, MD; David M. Holtzman, MD

Table 2. Sleep Measures and Nap Characteristics

Variable	Mean (SD)			95% CI of Group Differences
	All (n = 142)	Aβ42 Level >500 pg/mL (n = 110)	Aβ42 Level ≤500 pg/mL (n = 32)	
Sleep efficiency, %	82.9 (6.2)	83.7 (5.6)	80.4 (7.7)	0.8 to 5.7
Wake time after sleep onset, min	56.1 (22.6)	54.0 (21.8)	63.1 (23.9)	−17.9 to −0.21
Total sleep time, min	402.6 (44.6)	403.0 (47.3)	401.3 (49.0)	−16.0 to 19.5
Time in bed, min	486.4 (49.8)	482.3 (47.3)	500.6 (55.8)	−37.9 to 1.23
Nap days per week[a]	1.4 (1.7)	1.3 (1.6)	1.9 (1.9)	−1.3 to 0.1
Frequent naps (≥3 d per week), No. (%)	26 (18.4)[a]	16 (14.7)[a]	10 (31.2)	−0.32 to −0.01

JAMA Neurol. 2013;70(5):587-593

Sleep Fragmentation and the Risk of Incident Alzheimer's Disease and Cognitive Decline in Older Persons

Andrew S. P. Lim, MD[1]; Matthew Kowgier, PhD[2]; Lei Yu, PhD[3,4]; Aron S. Buchman, MD[3,4]; David A. Bennett, MD[3,4]

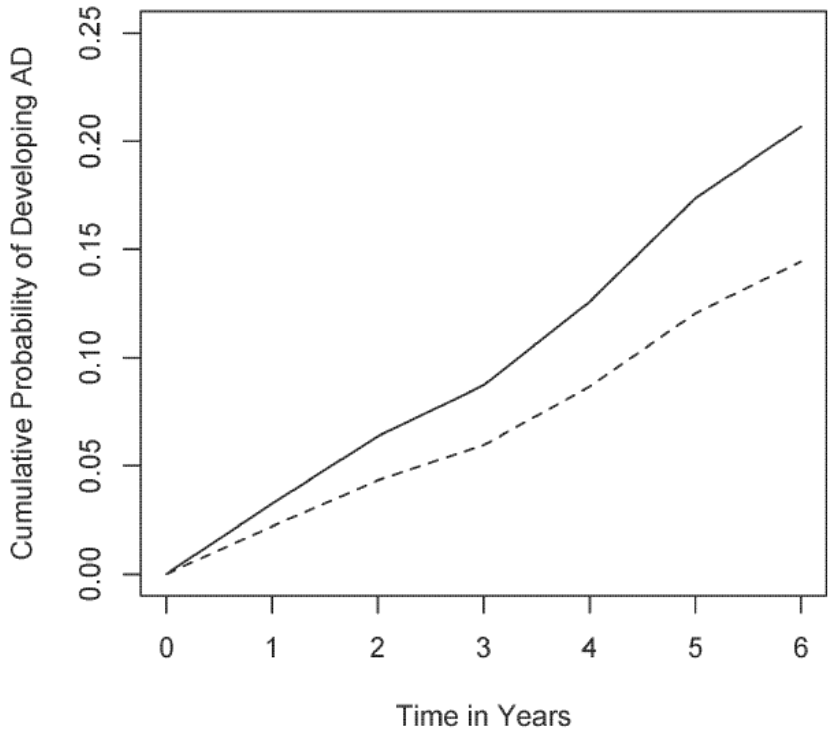


Figure 2—Expected risk of AD. The model predicted risk of AD based on the entire cohort is illustrated for two hypothetical average participants with high (Solid line: 90th percentile; k_{RA} = 0.036) and low (Dotted line: 10th percentile; k_{RA} = 0.021) levels of sleep fragmentation.

SLEEP 2013;36(7):1027-1032.

Introduction

- Sleep is a vital biological function, essential for brain restoration and memory consolidation

- Accumulating evidence suggests that sleep duration, sleep fragmentation or sleep pathologies as sleep disordered breathing can play a role in the pathogenic process leading to cognitive impairment

Sleep-Disordered Breathing, Hypoxia, and Risk of Mild Cognitive Impairment and Dementia in Older Women

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Alison M. Laffan, PhD
Stephanie Litwack Harrison, MPH
Susan Redline, MD, MPH
Adam P. Spira, PhD
Kristine E. Ensrud, MD
Sonia Ancoli-Israel, PhD
Katie L. Stone, PhD

Table 3. Mild Cognitive Impairment or Dementia Among Older Women According to Hypoxia, Sleep Fragmentation, or Sleep Duration Measures

	Mild Cognitive Impairment or Dementia, No. (%) (n = 107)	OR (95% CI)	
		Unadjusted	Adjusted[a]
Hypoxia and Disordered Breathing Measures			
Oxygen desaturation index, events/h			
<15	46 (43.0)	1 [Reference]	1 [Reference]
≥15	60 (56.1)	1.67 (1.03-2.69)	1.71 (1.04-2.83)
Oxygen saturation <90%			
<1% of sleep time	64 (59.8)	1 [Reference]	1 [Reference]
≥1% of sleep time	43 (40.2)	0.87 (0.54-1.41)	0.83 (0.51-1.38)
Sleep time in apnea or hypopnea, %			
Low (median: 0.9 [range, 0-2.2])	31 (29.0)	1 [Reference]	1 [Reference]
Mid (median: 4.4 [range, 2.3-7.0])	31 (29.0)	1.00 (0.55-1.82)	1.16 (0.61-2.20)
High (median: 16.4 [range, 7.0-66.8])	45 (42.1)	1.79 (1.01-3.20)	2.04 (1.10-3.78)

JAMA. 2011;306(6):613-619

Associations Between Sleep-Disordered Breathing, Nocturnal Hypoxemia, and Subsequent Cognitive Decline in Older Community-Dwelling Men: The Osteoporotic Fractures in Men Sleep Study

Terri Blackwell, MA,[a] Kristine Yaffe, MD,[b,c,d,e] Alison Laffan, PhD,[a] Susan Redline, MD, MPH,[f,g] Sonia Ancoli-Israel, PhD,[h,i] Kristine E. Ensrud, MD, MPH,[j,k] Yeonsu Song, PhD,[a] and Katie L. Stone, PhD,[a] for the Osteoporotic Fractures in Men Study Group

Table 4. Adjusted Association Between Sleep-Disordered Breathing Parameter and Clinically Significant Cognitive Decline

	Trail-Making Test Part B, Seconds	Modified Mini-Mental State Examination Score
Parameter	**Odds Ratio (95% Confidence Interval)**	
Apnea-hypopnea index, events/h		
<15 (n = 1,504)	Reference	Reference
≥15 (n = 1,132)	1.14 (0.84–1.54)	0.99 (0.79–1.24)
Continuous, per 5-unit increase	1.01 (0.96–1.07)	1.01 (0.97–1.05)
Oxygen desaturation index, events/h		
<15 (n = 1,219)	Reference	Reference
≥15 (n = 1,417)	1.05 (0.78–1.43)	0.95 (0.75–1.19)
Continuous, per 5-unit increase	1.02 (0.97–1.06)	1.01 (0.98–1.04)
Sleep time with oxygen saturation <90%, %		
<1 (n = 1,284)	Reference	Reference
≥1 (n = 1,352)	0.93 (0.68–1.27)	1.13 (0.90–1.43)
Continuous, per SD increase (9.45)	0.91 (0.76–1.10)	1.06 (0.95–1.18)
Sleep time in apnea or hypopnea, %		
Quartile 1: <4.6 (n = 659)	Reference	Reference
Quartile 2: 4.6 to <9.7 (n = 659)	0.88 (0.58–1.33)	0.90 (0.66–1.22)
Quartile 3: 9.7 to <18.4 (n = 659)	1.15 (0.77–1.73)	0.85 (0.62–1.17)
Quartile 4: ≥18.4 (n = 659)	0.96 (0.63–1.46)	0.90 (0.65–1.23)
Continuous, per SD increase (13.31)	1.05 (0.91–1.22)	1.01 (0.91–1.13)

J Am Geriatr Soc. 2015 Mar;63(3):453-61.

Introduction

- Sleep is a vital biological function, essential for brain restoration and memory consolidation

- Accumulating evidence suggests that sleep duration, sleep fragmentation or sleep pathologies as or sleep disordered breathing can play a role in the pathogenic process leading to cognitive impairment

- But most of the previous studies relied on self-reported sleep duration or rest-activity cycles measured by actigraphy

Sleep characteristics and cognitive impairment in the general population

The HypnoLaus study

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Nadia Tobback, RPSGT
Daniela Andries, RPSGT
Pedro Marques-Vidal, MD
Gérard Waeber, MD
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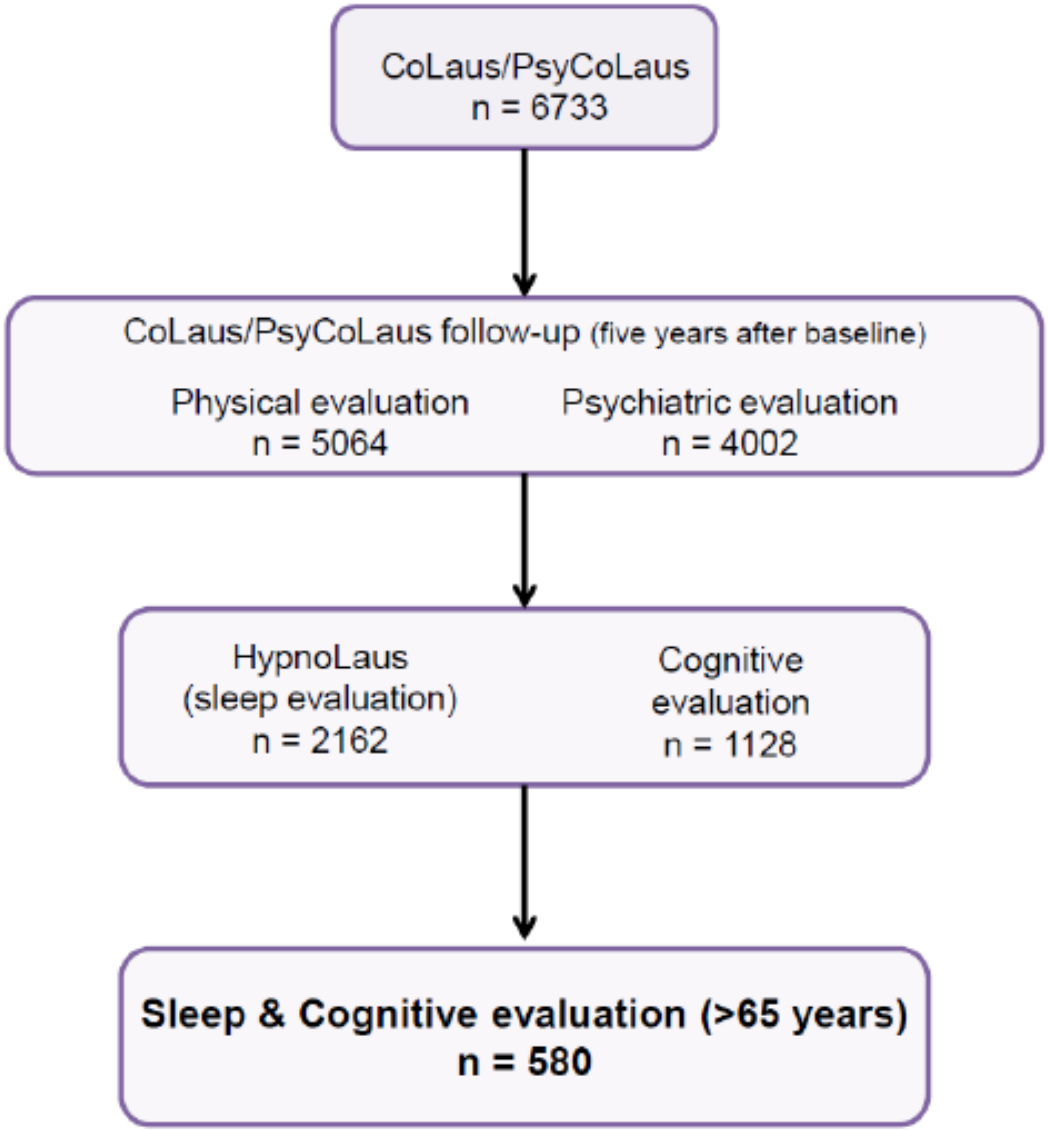
Raphaël Heinzer, MD, MPH*
Julius Popp, MD*

- We compared subjective sleep characteristics (assessed by questionnaires) and objective sleep characteristics (measured by PSG), in elderly participants (> 65 years old) with cognitive impairment vs. participants with normal cognition

Haba-Rubio *et al* Neurology® 2017;88:1-7



Haba-Rubio *et al* *Neurology®* 2017;88:1-7

- Battery of neuropsychological tests:
  - Mini Mental State Examination
  - Grober and Buschke Double Memory Test
  - DO 80 naming task
  - Stroop Test
  - Letter fluency task
  - Figures from the CERAD neuropsychological test battery

- Overall cognitive and functional status was determined using the Clinical Dementia Rating (CDR) scale

Composite Rating	Symptoms
0	none
0.5	very mild
1	mild
2	moderate
3	severe

Haba-Rubio *et al* Neurology® 2017;88:1-7

General characteristics, stratified by CDR status

TOTAAL N= 580	CDR = 0	CDR > 0	p value
N (%)	289 (49.8)	291 (50.1)	
Age, yrs	72.1±4.6	72.5±4.6	0.352
Gender, % women	65.7	43.3	**<0.001**
BMI, Kg/m²	26.7±4.5	27.2±4.7	0.135
Hypertension, %	61.9	73.4	**0.003**
Diabetes, %	13.8	22.3	**0.008**
Metabolic syndrome, %	40.1	46.7	0.109
Current depression, %	5.3	4.6	0.698
Depression in life, %	37.6	35.8	0.662

Haba-Rubio *et al* Neurology® 2017;88:1-7

Subjective sleep characteristics

	CDR = 0	CDR > 0	p value*
Subjective sleep latency, min	18.4±16.7	19.4±17.3	0.474
Estimated sleep duration, h	7.1±1.1	7.3±1.3	0.150
PSQI score	5.1±3.3	5.4±3.5	0.365
PSQI > 5, %	48.9	50.4	0.751
Epworth score	4.7±3.4	5.4±3.2	**0.024**
Epworth score >10%	6	5.3	0.723
Horne and Östberg questionnaire score	53.3±4.1	53.2±4.6	0.821
Berlin questionnaire score > 2, %	25.1	34	**0.019**

Haba-Rubio *et al* Neurology® 2017;88:1-7

Polysomnographic characteristics (I)

	CDR = 0	CDR > 0	p value*
Total sleep time, min	392.2±72.8	380.9±77.4	0.070
Sleep onset latency, min	21.2±28	22.1±25.1	0.300
Sleep efficiency, %	79.5±11.6	77.1±11.9	**0.007**
Stage 1, %	12.9±8.5	15.1±9.5	**0.004**
Stage 2, %	49.5±11.8	49.6±12.4	0.914
Stage 3, min	67.5±32.6	61±33.4	**0.018**
Stage 3, %	17.4±8.5	16.2±8.9	0.097
REM sleep, min	80±31	73.7±31.8	**0.016**
REM sleep, %	20.2±6.7	19.1±7	0.054
Wake after sleep onset, min	103.4±65.4	115±67.3	**0.018**
REM latency, min	105.9±81.6	102.6±71.5	0.779

Haba-Rubio *et al* Neurology® 2017;88:1-7

Polysomnographic characteristics (II)

	CDR = 0	CDR > 0	p value*
AHI, n/h	10.8±12.9	16±17.4	**<0.001**
Mean SaO_2, %	93.4±1.6	93.2±1.7	0.325
Lowest SaO_2, %	84.4±5.3	83.5±5.6	**0.029**
ODI, ≥ 3%	17.7±15.1	22.5±19.4	**0.007**
ODI, ≥ 4%	10±11.8	14.7±16.1	**0.001**
ODI, ≥ 6%	3.6±6.2	6.5±10.7	**<0.001**
Arousal index, n/h	24.2±11.8	26.7±14	0.102
PLMS index, n/h	22.9±28.7	26.4±36.7	0.848

Haba-Rubio *et al* Neurology® 2017;88:1-7

Association des variables polysomnographiques avec CDR > 0

	Odd ratio	95% CI	p value
Total sleep time, min	0.999	0.997-1.000	0.884
Sleep latency, min	0.997	0.990-1.004	0.466
Sleep efficiency, %	0.996	0.980-1.012	0.675
Stage 1, %	1.010	0.988-1.033	0.347
Stage 2, %	0.995	0.979-1.011	0.557
Stage 3, %	1.00	0.983-1.028	0.626
REM sleep, %	0.988	0.960-1.017	0.433

Multivariate logistic regression model adjusted for age, gender, hypertension, diabetes, metabolic syndrome, depression, lifetime depression, BMI, alcohol and tobacco consumption, drugs influencing sleep and level of education.

Haba-Rubio *et al* Neurology® 2017;88:1-7

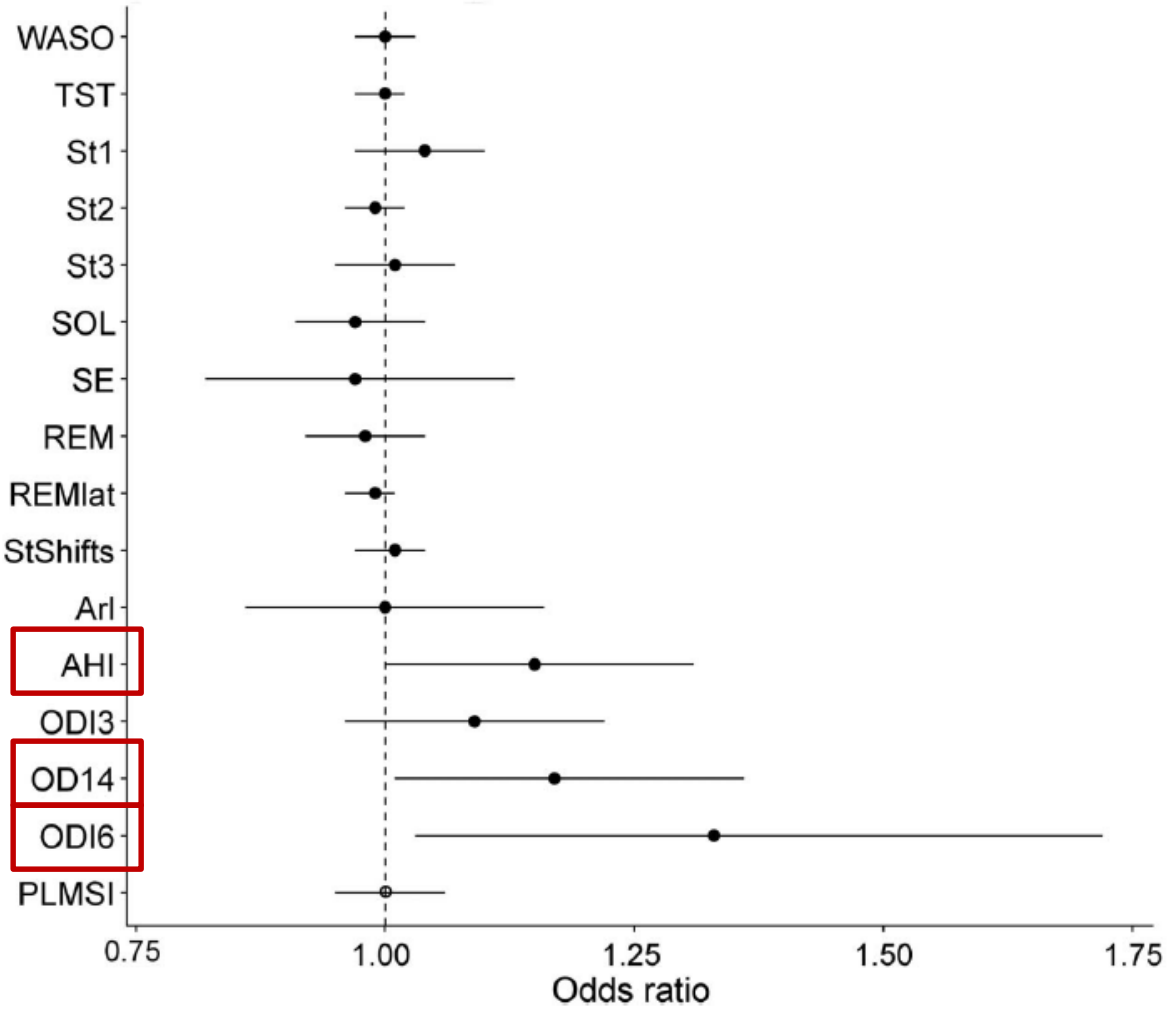
Association des variables polysomnographiques avec CDR > 0

	Odd ratio	95% CI	p value
AHI, n/h	1.013	1.000-1.027	**0.043**
Mean SaO_2, %	0.969	0.861-1.090	0.602
Lowest SaO_2, %	0.976	0.943-1.011	0.184
ODI ≥ 3%, n/h	1.008	0.996-1.020	0.173
ODI ≥ 4%, n/h	1.016	1.001-1.031	**0.033**
ODI ≥ 6%, n/h	1.028	1.002-1.055	**0.029**
Arousal index, n/h	1.000	0.985-1.015	0.993
PLMS index, n/h	1.000	0.994-1.006	0.885

Multivariate logistic regression model adjusted for age, gender, hypertension, diabetes, metabolic syndrome, depression, lifetime depression, BMI, alcohol and tobacco consumption, drugs influencing sleep and level of education.

Haba-Rubio *et al* Neurology® 2017;88:1-7

Figure 2 Association of polysomnographic variables with a Clinical Dementia Rating scale score >0, multivariate analysis



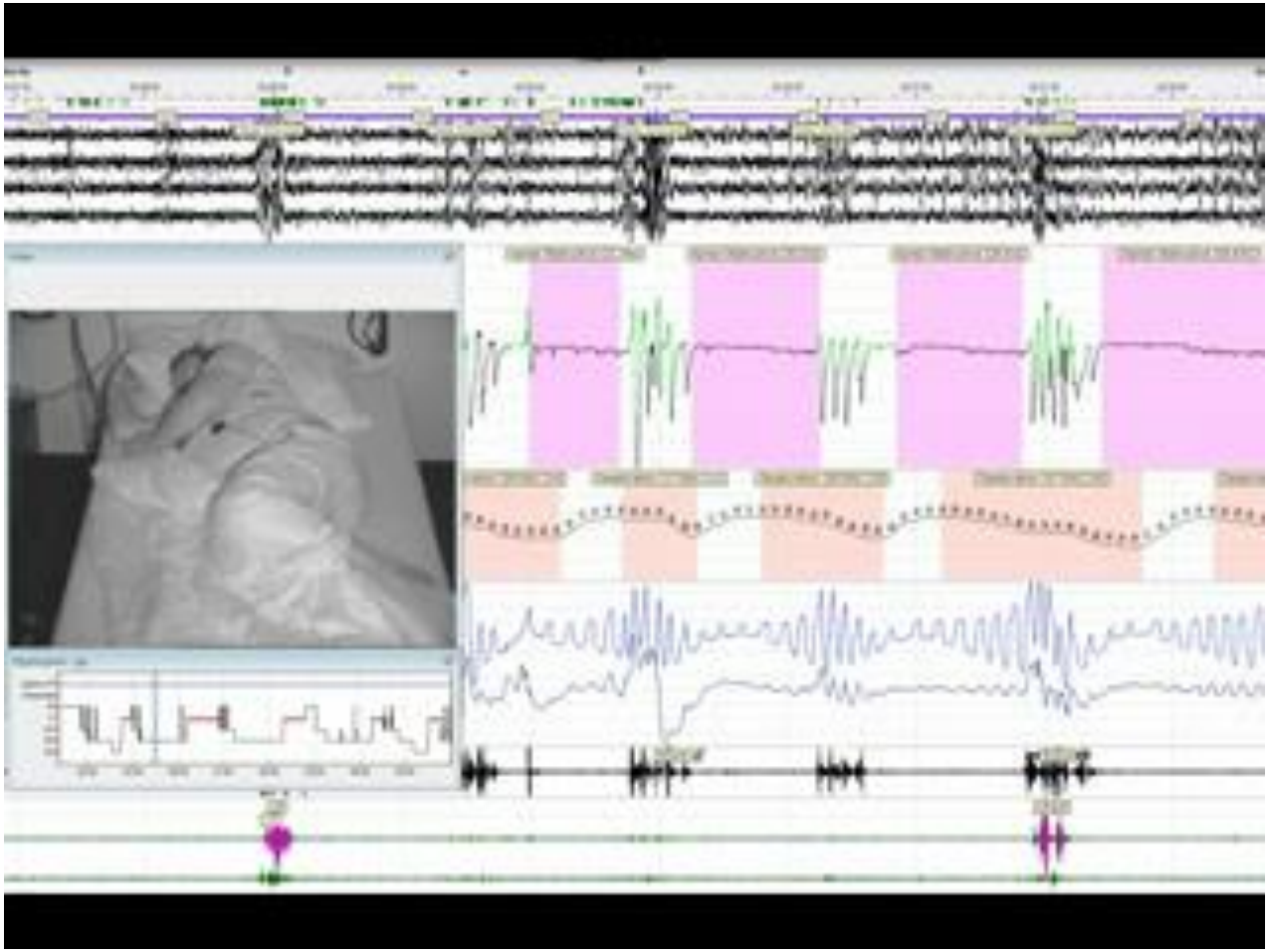
Multivariate logistic regression model adjusted for age, gender, hypertension, diabetes, metabolic syndrome, depression, lifetime depression, BMI, alcohol and tobacco consumption, drugs influencing sleep and level of education.

Haba-Rubio *et al* Neurology® 2017;88:1-7

- With increasing sleep apnea severity, measured by the AHI, we observed a worsening of specific cognitive scores, in particular:

  - the Grober and Buschke total free recall (r = -0.126, p = 0.004)
  - the Grober and Buschke delayed free recall (r = -0.092, p = 0.038)
  - semantic verbal fluency (r = -0.105, p = 0.017)
  - Stroop dots (r= -0.121, p = 0.004)

	CDR = 0 (n=289)	CDR > 0 (n=291)	p value
Memory tasks (Grober and Buschke)			
Immediate recall	16.36±4.46	15.85±2.74	0.120
Total free recall	33.82±4.87	26.23±6.91	**<0.001**
Total cued recall	17.30±11.26	19.56±8.54	**0.009**
Identification	15.96±0.50	15.93±0.43	0.549
Recognition	45.61±8.21	44.85±9.04	0.322
Delayed free recall	12.82±1.90	10.38±2.81	**<0.001**
Delayed cued recall	4.60±4.31	5.73±3.57	**0.001**
Other cognitive tasks			
Mini-Mental State Examination	28.91±3.03	28.45±2.30	0.201
CERAD figures	10.52±1.01	10.42±1.14	0.307
Semantic verbal fluency	31.72±8.24	27.94±7.80	**<0.001**
Phonemic verbal fluency	22.73±7.65	19.23±7.63	**<0.001**
Stroop dots condition	23.94±0.31	23.81±0.96	**0.039**
Stroop words condition	23.96±0.22	23.92±0.60	0.303
Stroop interference condition	23.30±1.80	23.10±1.80	0.193
DO40 naming task	39.85±0.48	39.65±1.26	**0.025**



Do diurnal cortisol levels mediate the association between sleep disturbances and cognitive impairment?

José Haba-Rubio[1], Sami Ouanes[2], Yannick Franc[3], Pedro Marques Vidal[4], Gerard Waeber[4], Peter Vollenweider[4], Armin von Gunten[2], Martin Preisig[2], Christine Kuehner[5], Enrique Castelao[2], Raphaël Heinzer[1], Julius Popp[2,6]

Table S3. Objective sleep characteristics and cortisol measures according to CDR (Clinical Dementia Rating [CDR]) status.

	CDR=0 N=233	CDR>0 N=207	p-value
Total sleep time, min	390.5 (77.3)	380.4 (77.1)	0.164
Sleep efficiency, %	78.7 (11.8)	76.1 (11.9)	0.012
Slow wave sleep (stage N3), min	67.5 (32.6)	60.7 (33.6)	0.016
REM sleep, min	79.8 (31.2)	73.9 (31.7)	0.049
Arousal index, n/h	24.4 (11.4)	27.3 (14.6)	0.093
Apnea/hypopnea index, n/h	11.5 (14.7)	16.0 (17.2)	0.001
ODI ≥3%, n/h	18.0 (16.4)	22.5 (19.3)	0.011
ODI ≥4%, n/h	10.5 (13.5)	14.7 (15.9)	0.002
ODI ≥6%, n/h	4.1 (8.3)	6.5 (10.7)	0.000
Cortisol AUC, µmol.h/L	307.9 (117)	322.0 (14)	0.429
Cortisol upon waking, nmol/L	19.3 (8.8)	19.9 (9.3)	0.764
Cortisol 30 minutes after waking, nmol/L	22.8 (11.5)	25.43 (12.4)	0.563
Cortisol at 11 am, nmol/L	10.9 (7.8)	12.53 (8.8)	0.054
Cortisol at 8 pm, nmol/L	4.1 (4.5)	4.93 (7)	0.287

Abbreviations: ODI: Oxygen desaturation index; AUC: Area under the curve. Values are mean±SD.

Haba-Rubio et al Neurobiol Aging. 2018;69:65-67

Conclusions

- We found that participants from the general population aged >65 with CI, compared to participants with no cognitive deficits, have a more disrupted sleep.
- This was associated with the occurrence of sleep-disordered breathing, SDB indices being the only ones to be independently associated with an increased risk of CI.
- Our results suggest that this relationship is related to the severity of the SDB-induced intermittent hypoxia (and not related with sleep fragmentation).

CPAP (continous positive airway pressure)

Sustained Use of CPAP Slows Deterioration of Cognition, Sleep, and Mood in Patients with Alzheimer's Disease and Obstructive Sleep Apnea: A Preliminary Study

Jana R. Cooke, M.D.[1,5]; Liat Ayalon, Ph.D.[2]; Barton W. Palmer, Ph.D.[2]; Jose S. Loredo, M.D.[1,5]; Jody Corey-Bloom, M.D., Ph.D.[4,5]; Loki Natarajan, Ph.D.[3]; Lianqi Liu, M.D.[2]; Sonia Ancoli-Israel, Ph.D.[2]

JCSM
Journal of Clinical Sleep Medicine
2009;5(4):305-309

Slowing of cognitive deterioration

Variable	CPAP+ (n = 5) Mean (SD)		CPAP− (n = 5) Mean (SD)		Effect size
	End of RCT	Follow-Up	End of RCT	Follow-Up	
HVLT	15.2 (7.2)	14.0 (7.9)	13.8 (6.4)	12.8 (4.9)	0.1
WAIS**	19.3 (2.5)	17.0 (8.2)	15.4 (4.6)	12.3 (7.4)	−1.9
Trails A	86.6 (120.1)	96.2 (115.3)	67.6 (26.9)	100.0 (64.5)	0.5
Trails B	95.8 (25.8)	87.8 (71.1)	247.8 (96.3)	249.6 (78.9)	−0.3
WCST	43.6 (13.4)	33.6 (25.4)	35.8 (9.4)	28.8 (22.2)	0.7
Stroop	8.0 (4.1)	18.8 (16.0)	5.3 (3.0)	2.8 (12.1)	−0.8
FAS Letter	24.6 (16.3)	25.4 (26.3)	26.4 (16.2)	19.8 (9.8)	−0.7
FAS Animal	13.2 (9.2)	11.4 (12.6)	11.6 (6.1)	9.2 (5.5)	−0.1
Digit Cancel	18.4 (9.0)	16.2 (14.3)	13.7 (1.5)	11.0 (5.8)	−0.2

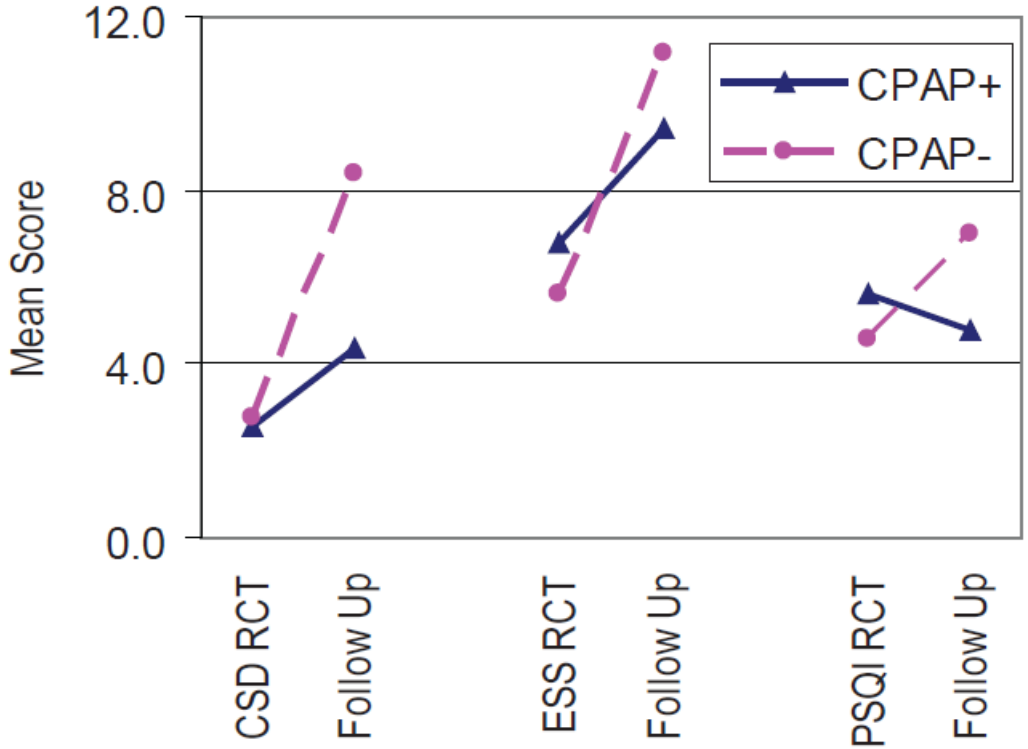
*Higher HVLT score implies more recall; Higher WAIS speed implies completing the task faster; Lower Trails A score implies completing the task faster; Lower Trails B score implies completing the task faster; Higher WCST score implies completing more of the task; Higher Stroop score implies being able to read more color/words; Higher FAS letter score implies the ability to think of more words; Higher FAS animal score implies the ability to think of more words; Higher Digit cancellation score implies completing more of the task. **p value = 0.06 from the Student's *t*-test and Mann-Whitney test.

Sustained Use of CPAP Slows Deterioration of Cognition, Sleep, and Mood in Patients with Alzheimer's Disease and Obstructive Sleep Apnea: A Preliminary Study

Jana R. Cooke, M.D.[1,5]; Liat Ayalon, Ph.D.[2]; Barton W. Palmer, Ph.D.[2]; Jose S. Loredo, M.D.[1,5]; Jody Corey-Bloom, M.D., Ph.D.[4,5]; Loki Natarajan, Ph.D.[3]; Lianqi Liu, M.D.[2]; Sonia Ancoli-Israel, Ph.D.[2]

JCSM
Journal of Clinical Sleep Medicine
2009;5(4):305-309

Positive effects on depression, sleepiness and overall sleep quality



FUTURE DIRECTIONS

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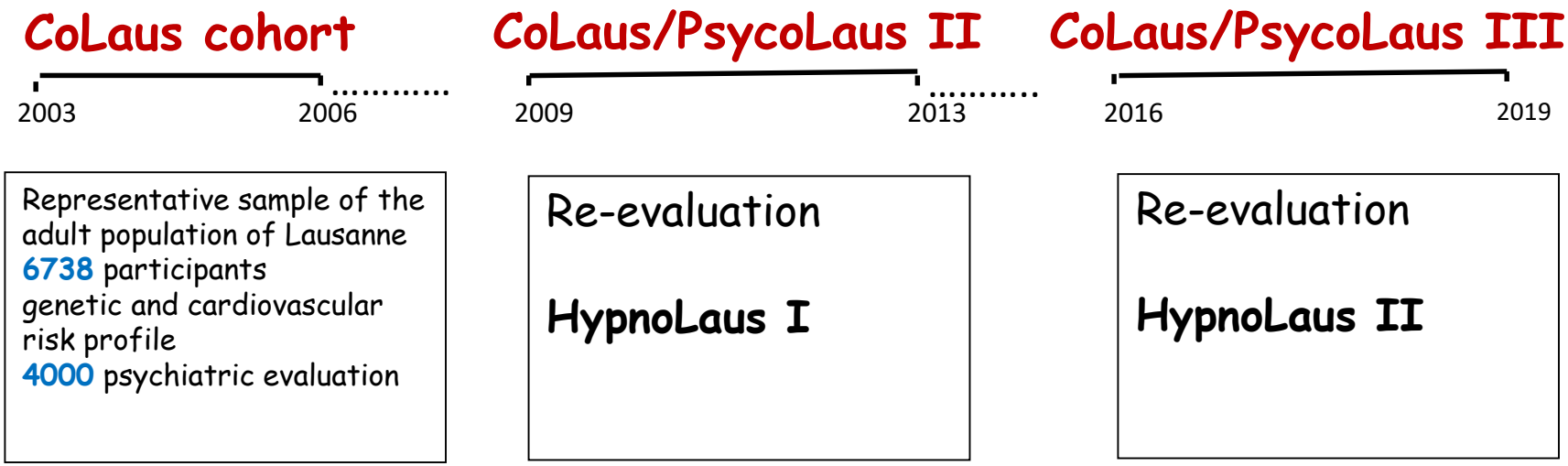
CENTRE DU SOMMEIL
DE FLORIMONT

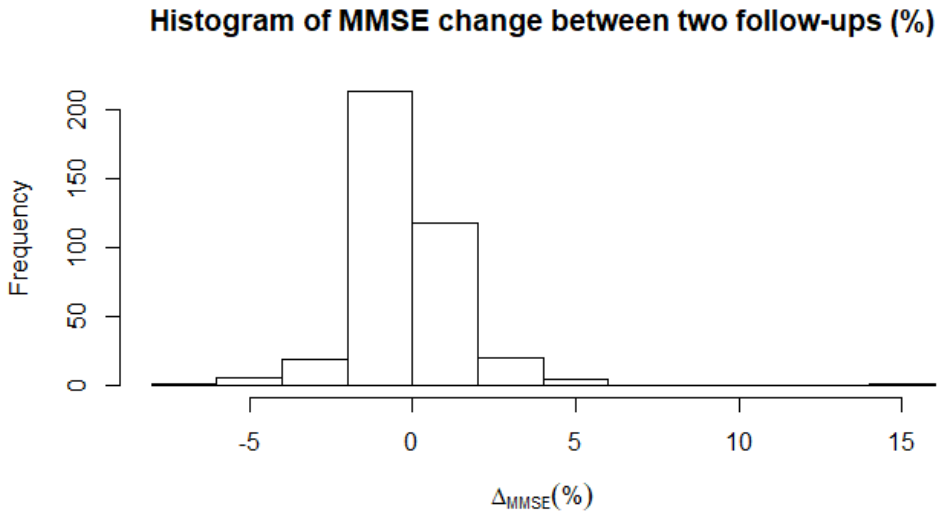
CoLaus/PsycoLaus follow-up



Prospective data of CoLaus/PsyCoLaus will be an unique opportunity to study the impact of sleep on health

Cognitive decline based on MMSE change

- Considering individuals with $\Delta_{MMSE} \geq 2$ as individuals with cognitive decline.
- The total number of individuals in the current sample is 380 with age range of 63.73, 81.38. The total number of individuals in the current sample is 380 with age range of 63.73, 81.38.



HypnoLaus, unpublished data

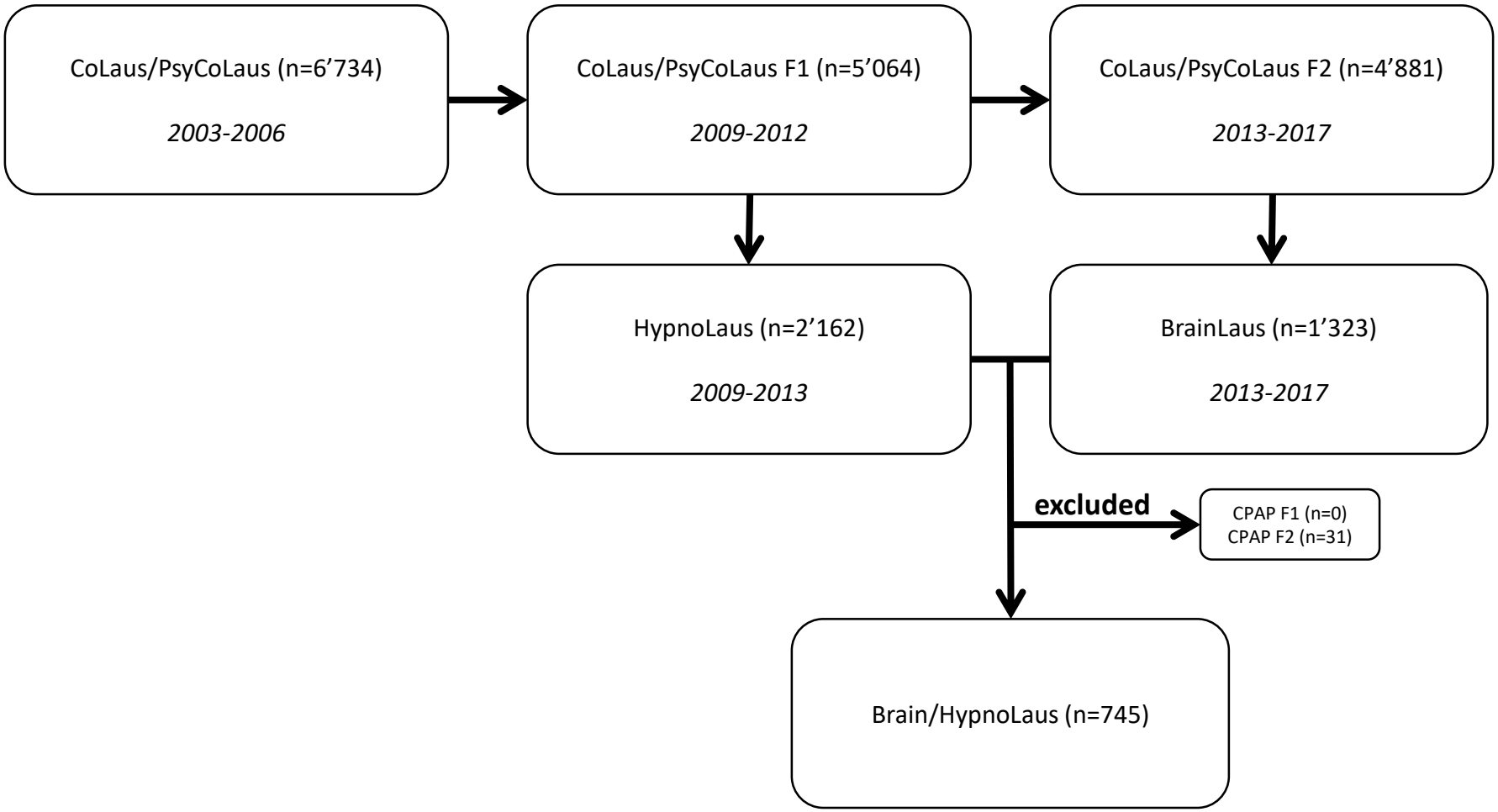
Results of linear regression models.

	Dependent variable:				
	Cognitive decline				
	(1)	(2)	(3)	(4)	(5)
FU1_mmesc	0.615**	0.605**	0.595**	0.591**	0.557**
	(0.242)	(0.241)	(0.247)	(0.234)	(0.240)
FU1_CL_age	0.055	0.042	0.047	0.056	0.054
	(0.034)	(0.035)	(0.036)	(0.034)	(0.037)
factor(FU1_SEX)1	-0.338	-0.453	-0.504	-0.486	-0.592*
	(0.306)	(0.300)	(0.310)	(0.299)	(0.335)
FU1_CL_BMI	0.050	0.033	0.048	0.069*	0.049
	(0.036)	(0.038)	(0.038)	(0.036)	(0.043)
FU1_MDD_current	-0.503	-0.454	-0.311	-0.366	-0.588
	(0.813)	(0.799)	(0.801)	(0.803)	(0.838)
ahi13					-0.023
					(0.015)
odi6	0.024*				0.053**
	(0.014)				(0.025)
meanspo2		-0.208**			-0.279*
		(0.094)			(0.158)
tstspo290			0.011		-0.011
			(0.009)		(0.015)
APNE_treatment				-0.657	-1.100
				(0.572)	(0.688)

Note: *p<0.1; **p<0.05; ***p<0.01

HypnoLaus, unpublished data

BrainLaus: brain imaging by MRI

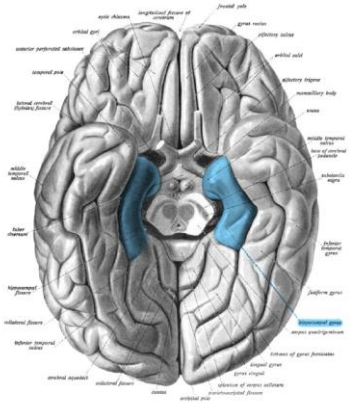


HypnoLaus, unpublished data

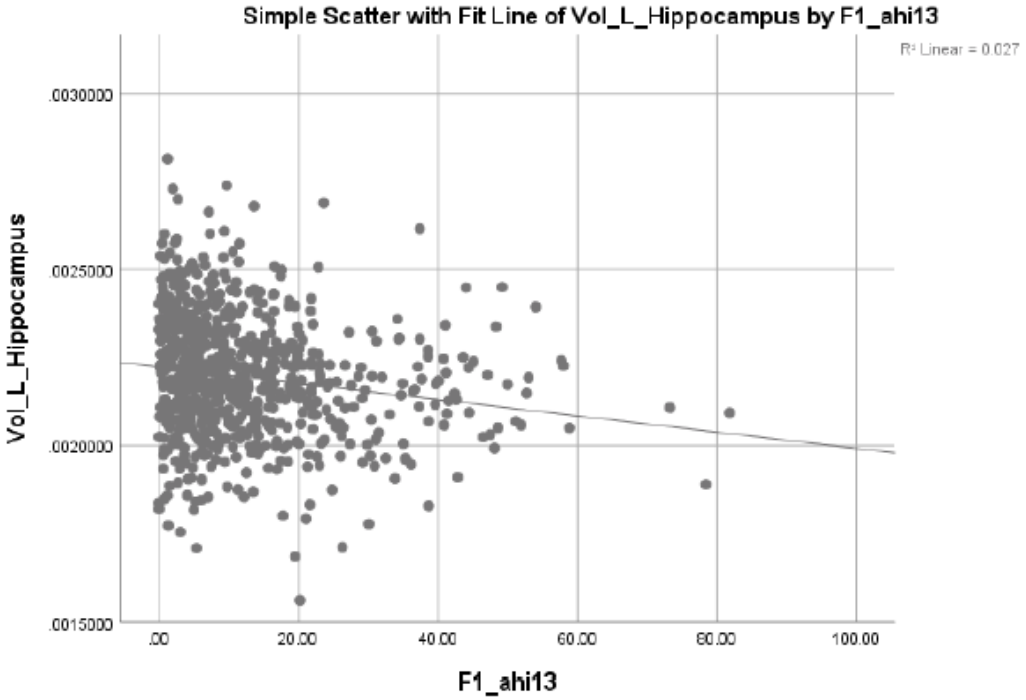
MRI volume characteristics stratified by AHI (< or > 15/h)

	Total (n=745)	Control (n=524, 70.3%)	SDB (n=221, 29.7%)	p value
Total grey matter (% of ICV)	41.62, 2.28	41.89, 2.33	40.96, 2.04	**<0.001**
R grey matter	20.70, 1.13	20.84, 1.15	20.38, 1.03	**<0.001**
L grey matter	20.91, 1.16	21.05, 1.19	20.58, 1.02	**<0.001**
R hippocampus	0.2329, 0.0176	0.2346, 0.0180	0.2290, 0.0162	**<0.001**
L hippocampus	0.2195, 0.0171	0.2212, 0.0173	0.2154, 0.0159	**<0.001**
R entorhinal area	0.1175, 0.0098	0.1183, 0.0096	0.1156, 0.0099	**0.001**
L entorhinal area	0.1155, 0.0105	0.1164, 0.0105	0.1132, 0.0101	**<0.001**
R parahippocampal gyrus	0.2034, 0.0132	0.2042, 0.0.132	0.2017, 0.0130	**0.018**
L parahippocampal gyrus	0.2204, 0.0143	0.2216, 0.0144	0.2176, 0.0138	**0.001**

Values are mean (SD) or n (%). Test: Independent T test → means.



HypnoLaus, unpublished data

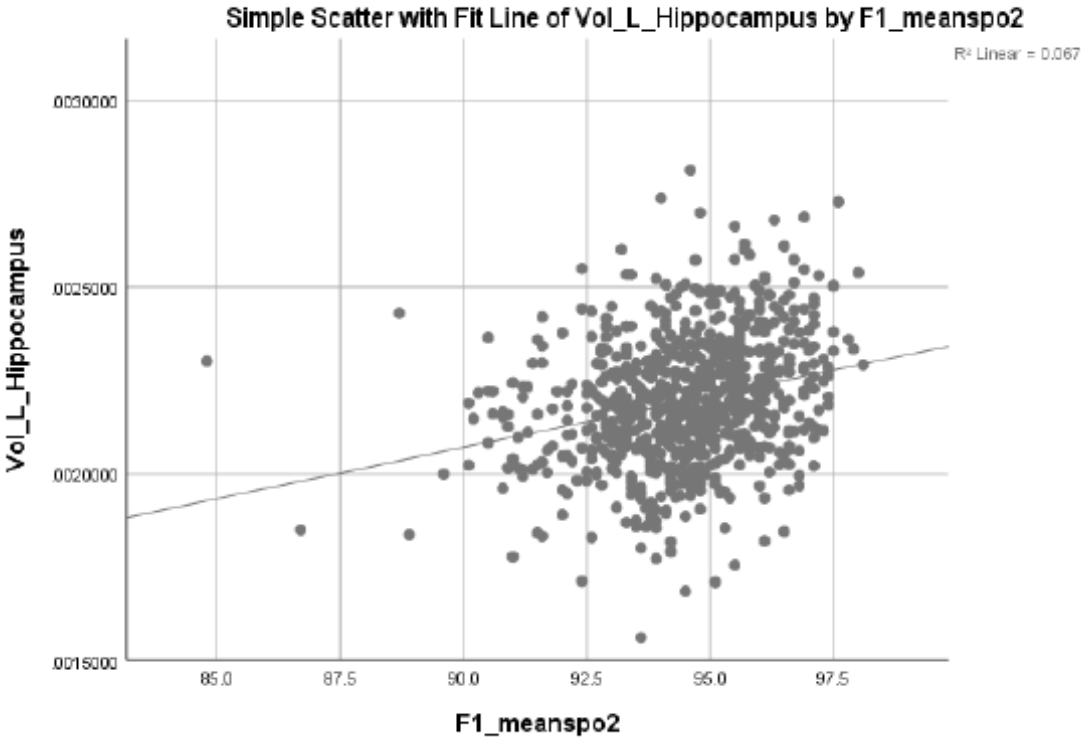


Correlations

		F1_ahi13	Vol_R_Hippocampus
F1_ahi13	Pearson Correlation	1	-.158**
	Sig. (2-tailed)		.000
	N	746	746
Vol_R_Hippocampus	Pearson Correlation	-.158**	1
	Sig. (2-tailed)	.000	
	N	746	746

**. Correlation is significant at the 0.01 level (2-tailed).

HypnoLaus, unpublished data



Correlations

		F1_meanspo2	Vol_L_Hippocampus
F1_meanspo2	Pearson Correlation	1	.259**
	Sig. (2-tailed)		.000
	N	745	745
Vol_L_Hippocampus	Pearson Correlation	.259**	1
	Sig. (2-tailed)	.000	
	N	745	746

**. Correlation is significant at the 0.01 level (2-tailed).

HypnoLaus, unpublished data

Volume Hyppoccampus

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
		B	Std. Error	Beta	t	Sig.	Lower Bound	Upper Bound
1	(Constant)	.001	.000		1.940	.053	.000	.002
	age_mri	-5.565E-6	.000	-.317	-8.508	.000	.000	.000
	gender (0=M, 1=F)	9.891E-5	.000	.289	8.508	.000	.000	.000
	F2_bmi	5.069E-6	.000	.124	3.395	.001	.000	.000
	F2_hta	-2.597E-7	.000	-.001	-.020	.984	.000	.000
	F2_diab	4.562E-5	.000	.059	1.780	.075	.000	.000
	F2_dyslip	1.932E-5	.000	.054	1.576	.115	.000	.000
	F1_meanspo2	1.623E-5	.000	.151	3.978	.000	.000	.000

a. Dependent Variable: Vol_L_Hippocampus

HypnoLaus, unpublished data

Table 3b: Multiple linear regression (ANOVA) → meanO2

Dependent variable (Vol)	Model 1 (age, gender)	Model 2 (age, gender, whratio, hta, diab, dyslip, smokeF1)	Model 3 (age, gender, bmi, hta, diab, dyslip, smokeF1)
Total GM	P 0.121, R2 28.8	0.156, 29.2	0.059
R GM	P 0.110, R2 29.0	0.156, 29.6	0.059
L GM	P 0.138, R2 28.0	0.161, 28.4	0.061
R hippocampus	**P 0.025, R2 21.0, OR 1.08**	**0.014, 21, OR 1.10**	**0.001, 22.8**
L hippocampus	**P 0.016, R2 21.6, OR 1.09**	**0.005, 22.8, OR 1.12**	**0.001, 22.4**
R entorhinal area	P 0.169, R2 16.7	0.203, 17.3	0.132
L entorhinal area	P 0.071, R2 16.1	0.159, 16.9	**0.045, 17.1**
R PHG	P 0.892, R2 11.0	0.321, 12.8	0.126
L PHG	P 0.524, R212.4	0.207, 13.6	0.062

HypnoLaus, unpublished data

Take home messages

- Data of HypnoLaus provide an unique opportunity to study the impact of sleep on health
- Sleep is influenced by many factors: age, gender, socio-economic status, environmental factors,…and sleep disorders
- Sleep disorders are very frequent in the general population

- Sleep disordered breathing (and in particular hypoxia) seems to be associated with cognitive impairment
  - Target to slow cognitive decline ?