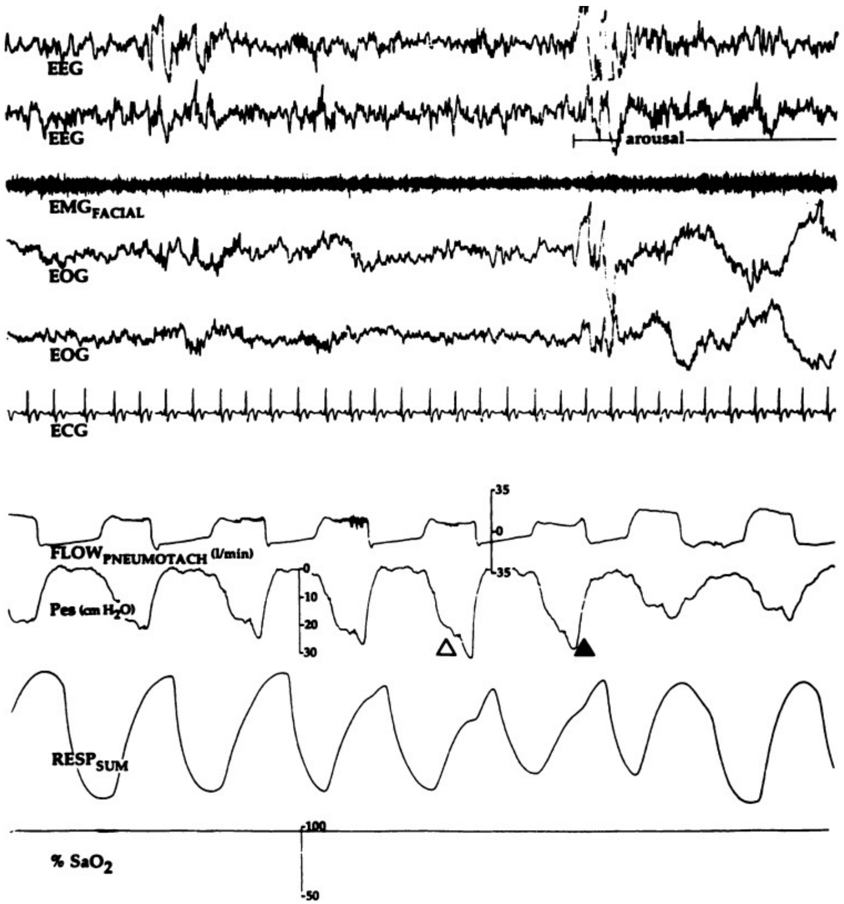
Syndrome de Haute Resistance des Voies Aériennes Supérieures : Une cause de fatigue chronique ? Faut-il la dépister ?

Dr Jean-Benoît MARTINOT

[1]Sleep Laboratory, CHU Université Catholique de Louvain (UCL) Namur Site Sainte-Elisabeth,

[2]Institute of Experimental and Clinical Research, UCL Bruxelles Woluwe, Brussels, Belgium

A Cause of Excessive Daytime Sleepiness
The Upper Airway Resistance Syndrome



Monitoring of an alpha EEG arousal with quantitative evaluation of airflow. Flow is measured with a tightly fitting mask and a heated pneumotachograph (channel 7 from top). Esophageal pressure (channel 8) is at its nadir in the two breaths just preceding the arousal (indicated by arrows). The arousal begins with the second Pes nadir. Immediately following the onset of the transient arousal, inspiratory Pes nadir is less negative (breath just following black arrow). The "sum" signal of inductive respiratory plethysmography presents some change in shape. However, this change would be difficult to interpret if Bowand Pes were not simultaneously measured . No desaturation is noted in the pulse oximetry recording. The Bow (channel 1) decreased the most in the breath just preceding the arousal (black arrow) but is already decreasing in the breath marked by the white arrow

Guilleminault C. et al. *CHEST* 1993

Table 1—*Population With Upper Airway Resistance Syndrome**

Subject No./ Age, yr/ Sex	Snoring	BMI, kg/m²	Night 1 Baseline TST, min	Night 1 Baseline Alpha EEG Arousal Index	Night 1 Baseline MSLT, min	Night 3 Baseline (w/Pes) TST, min	Night 3 Baseline (w/Pes) Alpha EEG Arousal Index	Night 3 Baseline (w/Pes) Maxi-mum Pes Nadir, cm H_2O	CPAP Titration Maximum Pes Nadir, cm H_2O	Follow-up CPAP Night Alpha EEG Arousal Index	Follow-up CPAP Night TST, min	Follow-up CPAP Night MSLT, min
1/30/F	+	32	481	33	2.3	492	35	−27	−8	9	398	9
2/42/F	+	28	473	31	2.8	460	30	−34	−6	10	393	10
3/40/F	0	20	492	19	5	478	23	−29	−4	8	406	12.8
4/39/F	0	24	468	36	6.1	490	34	−43	−5	6.1	389	14.5
5/24/F	+	22	501	17	6	452	23	−37	−4	6	411	14.6
6/36/F	+	21	497	52	8.1	450	46	−41	−5	0.8	381	17
7/46/F	Int	24	479	35	6.4	495	38	−36	−4.5	7	398	15.4
8/35/F	+	23	486	24	7	479	26	−33	−6	10	428	15.2
9/50/M	+	23	469	14	6.3	453	19	−23	−4	8	395	14.7
10/47/M	+	23	485	20	4	511	22	−25	−5	8	387	11.8
11/30/M	Int	23	499	42	4.7	442	38	−43	−5.5	9	401	13.5
12/19/M	+	19	471	16	5	473	18	−31	−5	6	389	14.8
13/44/M	+	23	465	40	5.1	434	44	−28	−6	9	386	12.5
14/41/M	Int	22	456	42	6.0	472	31	−24	−6	9	419	13.8
15/39/M	+	26	484	49	5.1	509	37	−42	−5	6	413	12.6
Mean 37.5		23.6	480.4	31.3	5.3	472.7	30.9	−33.1	−5.3	7.9	399.6	13.5
SD 7.0		3.2	12.93	12.4	1.5	24.7	9.2	7.1	1.1	2.3	15	2.1

Upper airway resistance syndrome-one decade later

Bao G. and Guilleminault C. *Cur. Opin. Pulm. Med.* 2004

Table 1. Clinical differential features in upper airway resistance syndrome (UARS) and obstructive sleep apnea-hypopnea syndrome (OSAHS)

Feature	UARS	OSAHS
Age	All ages	Children Male > 40 y old Female after menopause
Male:female ratio	1:1	2:1
Sleep onset	Insomnia	Fast
Snoring	Common	Almost always
Apnea	No	Common
Daytime symptoms	Tiredness Fatigue	Sleepiness (less common in children)
Body habitus	Slim or normal	Obese
Somatic functional complaints	Fibromyalgia Chronic pain Headaches	Rare
Orthostatic symptoms	Cold hands/feet Fainting Dizziness	Rare
Blood pressure	Low or normal	High
Neck circumference	Normal	Large

Table 2. Polysomnography and power spectral analysis in upper airway resistance syndrome (UARS) and obstructive sleep apnea-hypopnea syndrome (OSAHS)

	UARS	OSAHS
Sleep onset latency	Long	Short
AHI	< 5	≥ 5
Minimum O_2 saturation	$> 92\%$	Often $< 92\%$ (rare in children)
Respiratory effort-related arousals	Predominant	Minimal
Cyclic alternating patterns	Frequent	Less common
Power spectral EEG analysis	Higher α power Higher δ in rapid eye movement	Less α or δ

AHI, apnea-hypopnea index as events per hour.

Guilleminault C, Stoohs R, Shiomi T, Kushida C, Schnittger I. Upper airway resistance syndrome, nocturnal blood pressure monitoring, and **borderline hypertension**. Chest 1996;109:901–8.

American Thoracic Society. Sleep apnea, sleepiness, and **driving risk.** Am J Respir Crit Care Med 1994;150:1463–73.

Mitler MM, Miller JC, Lipsitz JJ, Walsh JK, Wylie CD.
Silverberg DS, Oksenberg A. **Essential hypertension** and abnormal upper airway resistance during sleep. Sleep 1997;20:794–806.

The sleep of long-haul **truck drivers**. N Engl J Med 1997;337:755–61.

Fleetham JA. A wake up call for sleep disordered breathing. Br Med J 1997;314:839–40. **EDS**
Guilleminault C, Davis K, Huynh NT. Prospective randomized study of patients with **insomnia** and mild sleep disordered breathing. Sleep 2008;31:1527–33.

Tantrakul V, Park CS, Guilleminault C. Sleep-disordered breathing in premenopausal women: differences between younger (less than 30 years old) and older women. Sleep 2012;13:656–62.**QoL**

Eckert DJ, Younes MK. Arousal from Sleep: implications for obstructive sleep apnea pathogenesis and treatment. J Appl Phys 2014;116:302–13. **Insomnia Fatigue**

An Official American Thoracic Society Workshop Report: Noninvasive Identification of Inspiratory Flow Limitation in Sleep Studies Ann Am Thorac Soc 2017; 14(7): 1076-1085.

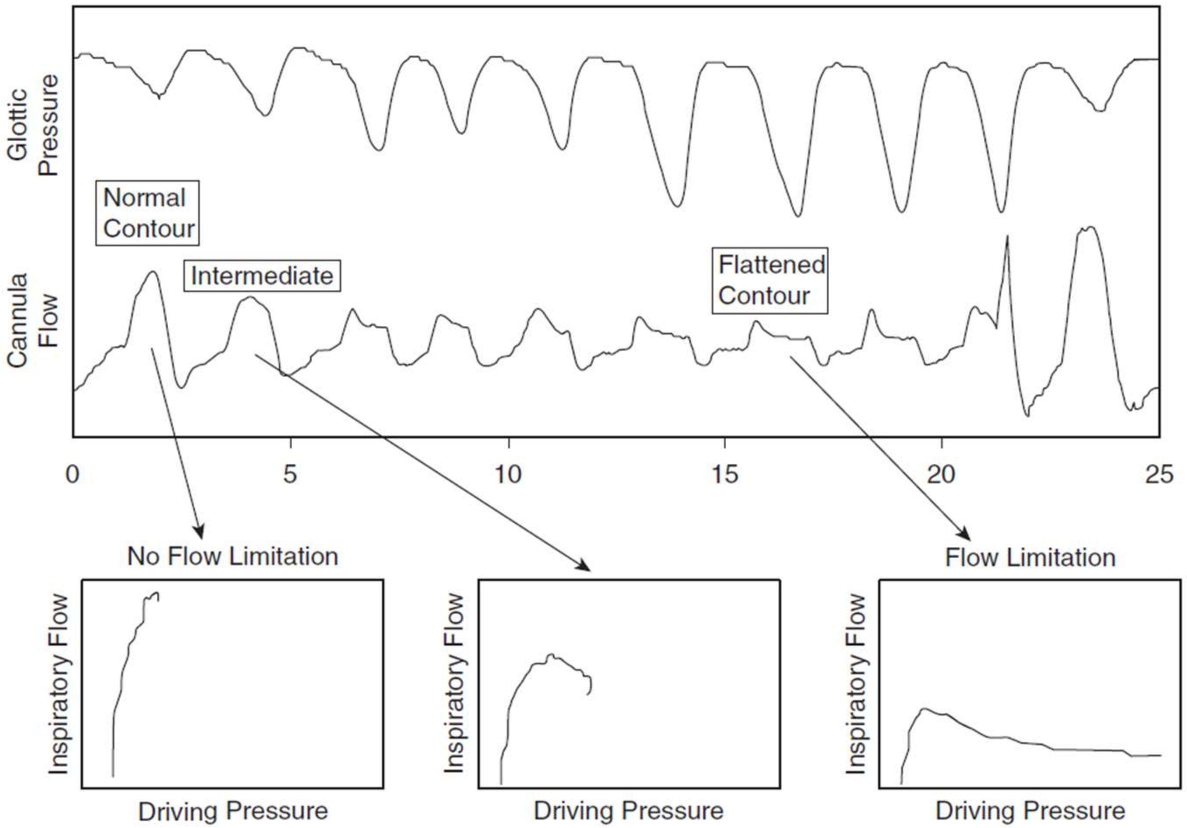
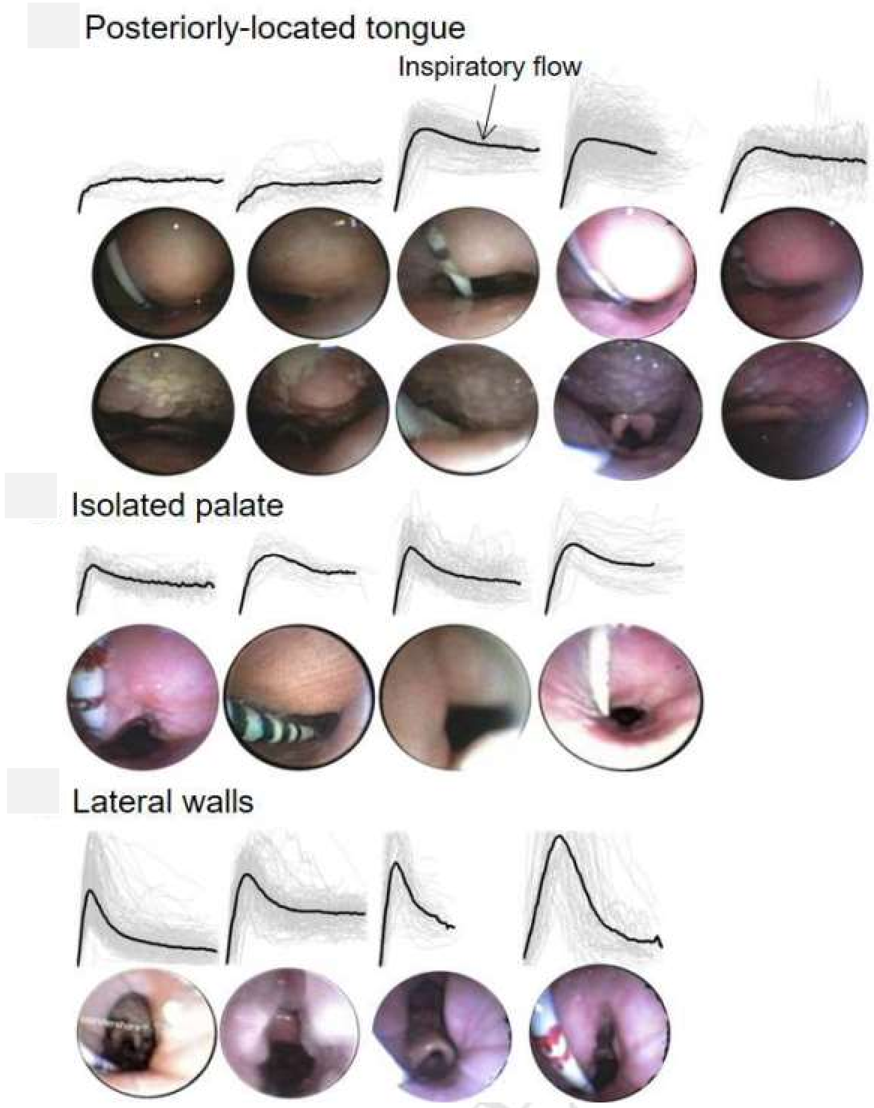
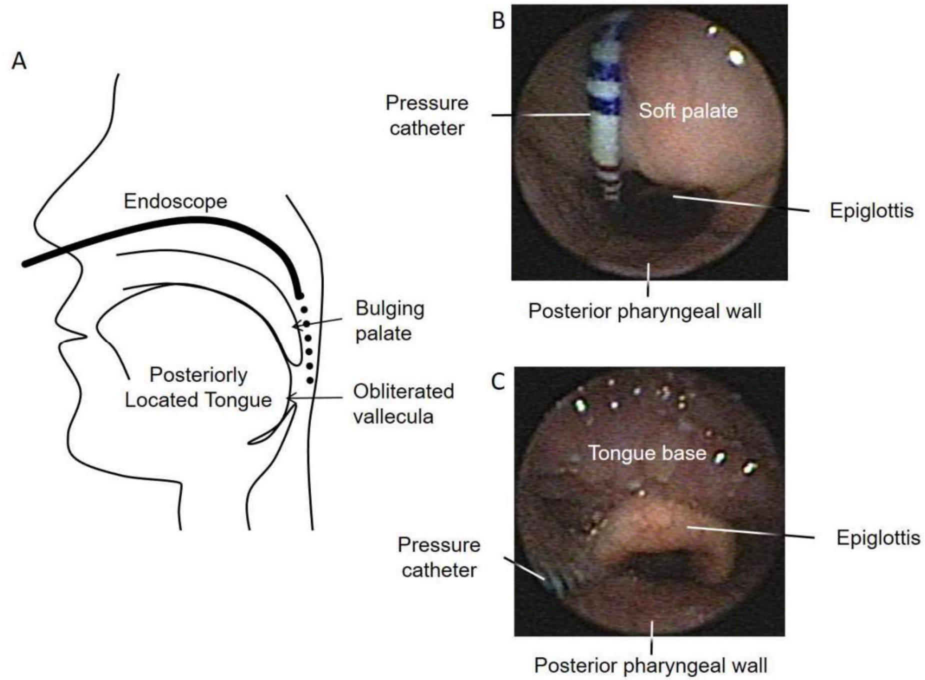


Figure 1. Flattening is shown pictographically here in a nasal cannula flow tracing. Flow-limited breaths, characterized by flattening, demonstrate a nonlinear relationship between driving pressure and flow in contrast to normal-contour breaths. Reprinted by permission from Reference 1.

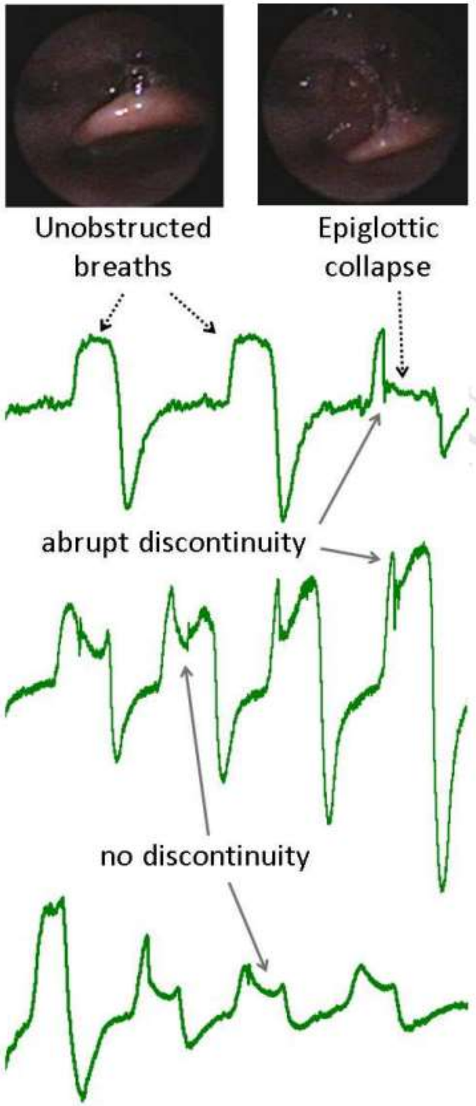
Airflow shape is associated with the pharyngeal structure causing obstructive sleep apnea

Genta PR. et al. *CHEST* 2017





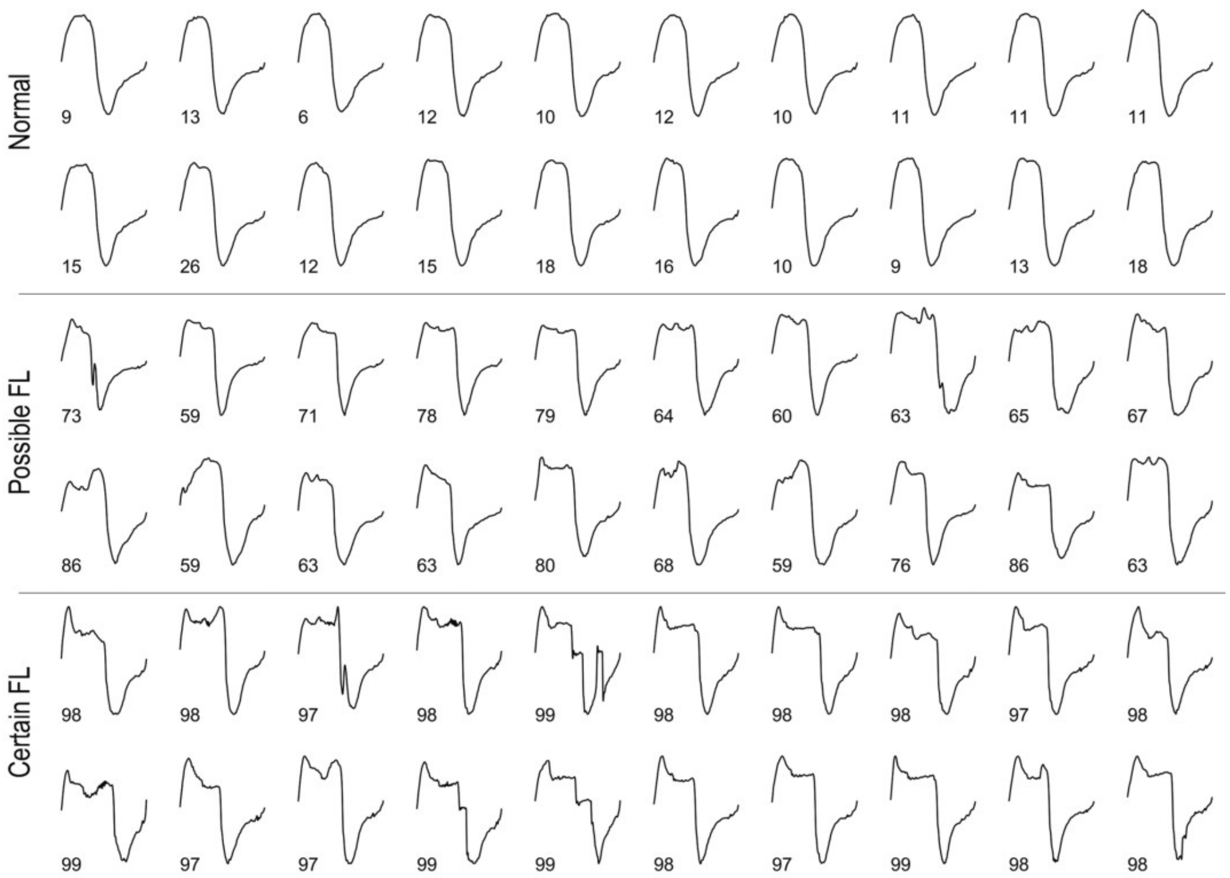
Airflow shape is associated with the pharyngeal structure causing obstructive sleep apnea



Representative examples of epiglottic collapse taken from different subjects. Epiglottic collapse is characterized by severe NED with and without abrupt discontinuities.

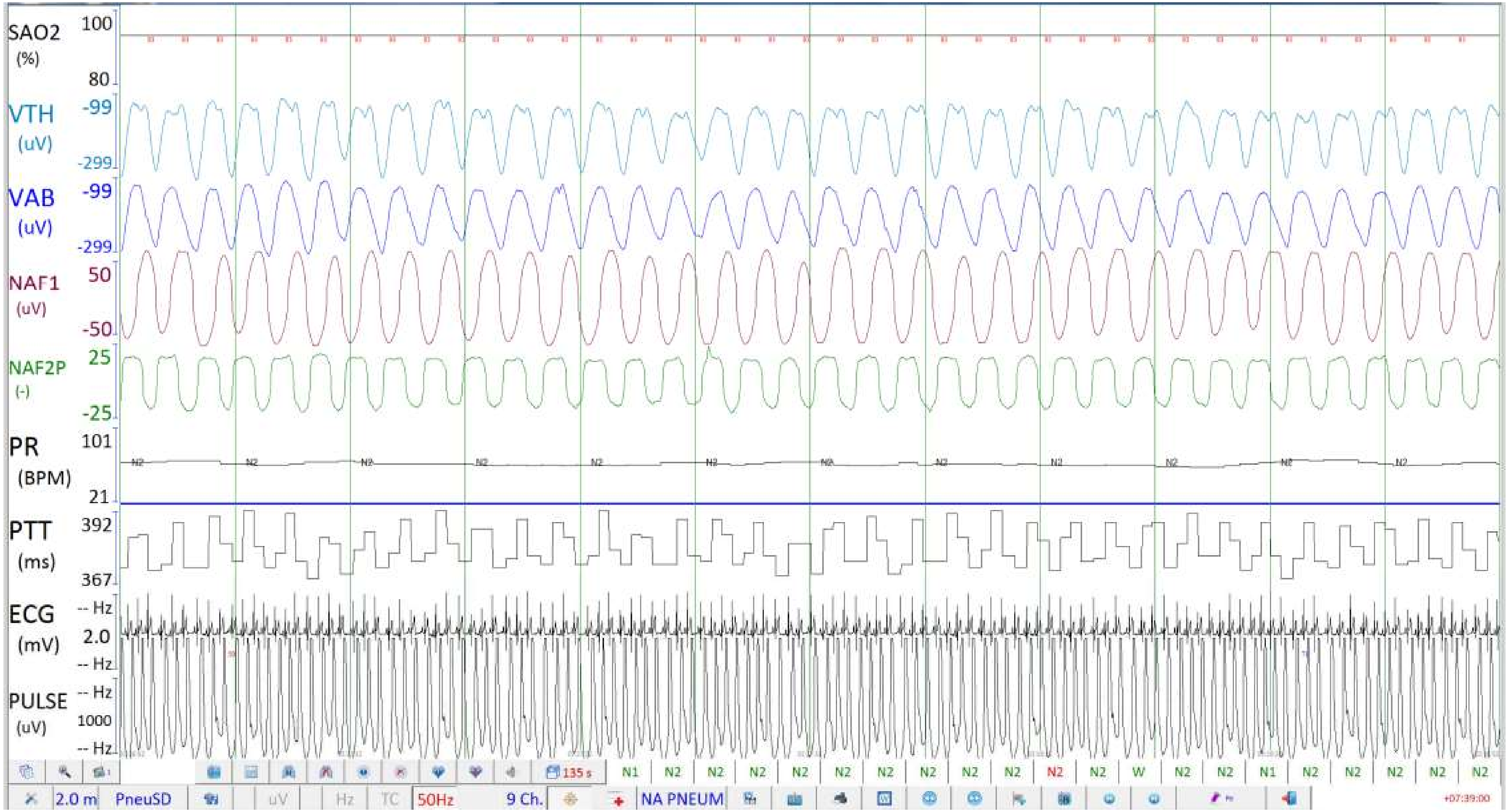
Genta PR. et al. *CHEST* 2017

Frequency of flow limitation using airflow shape

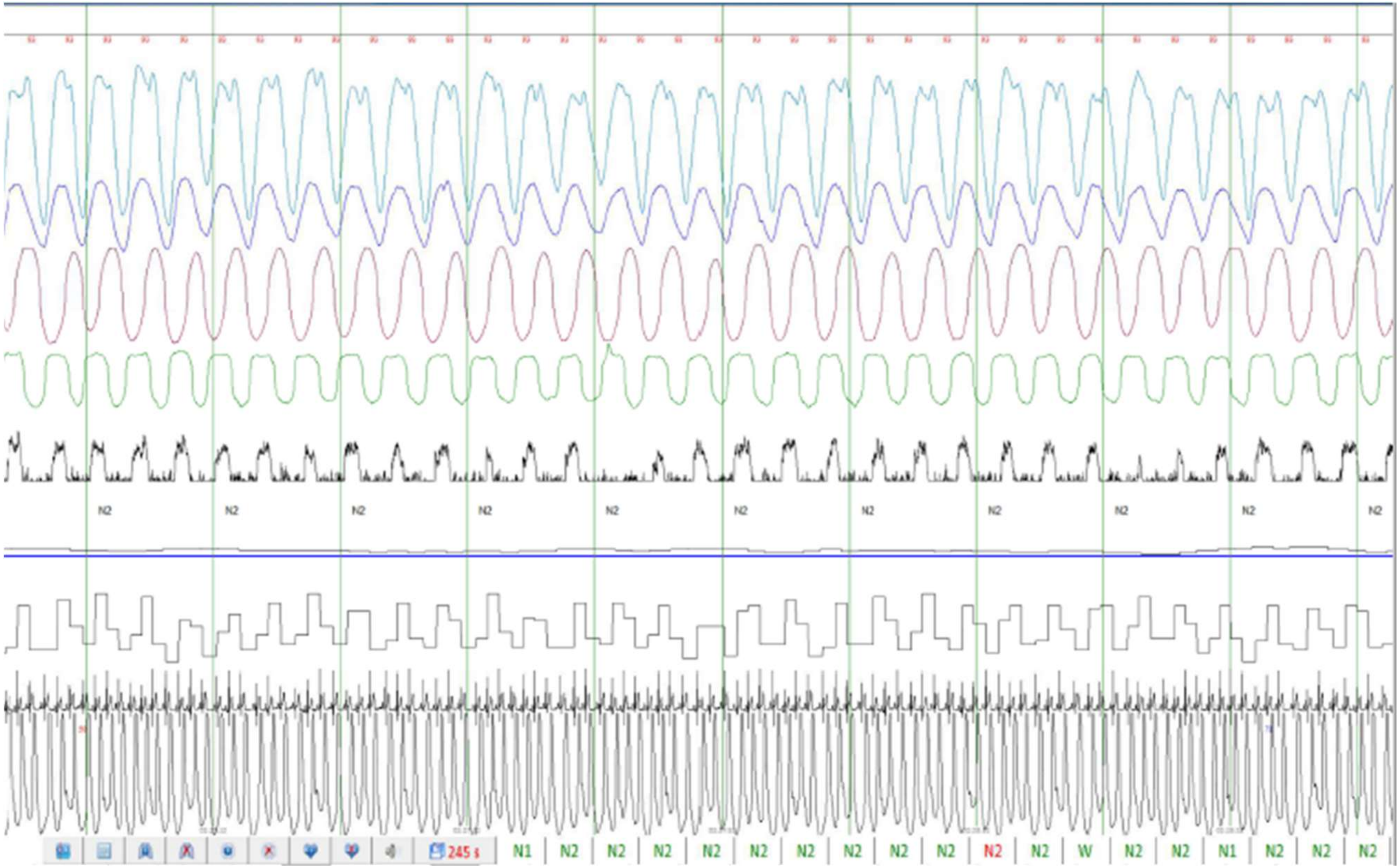


Example pneumotach flow traces for breaths visually scored as normal, possible flow limitation “Possible FL,” and certain flow limitation “Certain FL” for an individual patient. Note also the heterogeneity in shapes for breaths within this single subject.

Mann D.L. et al. *SLEEPJ* 2021

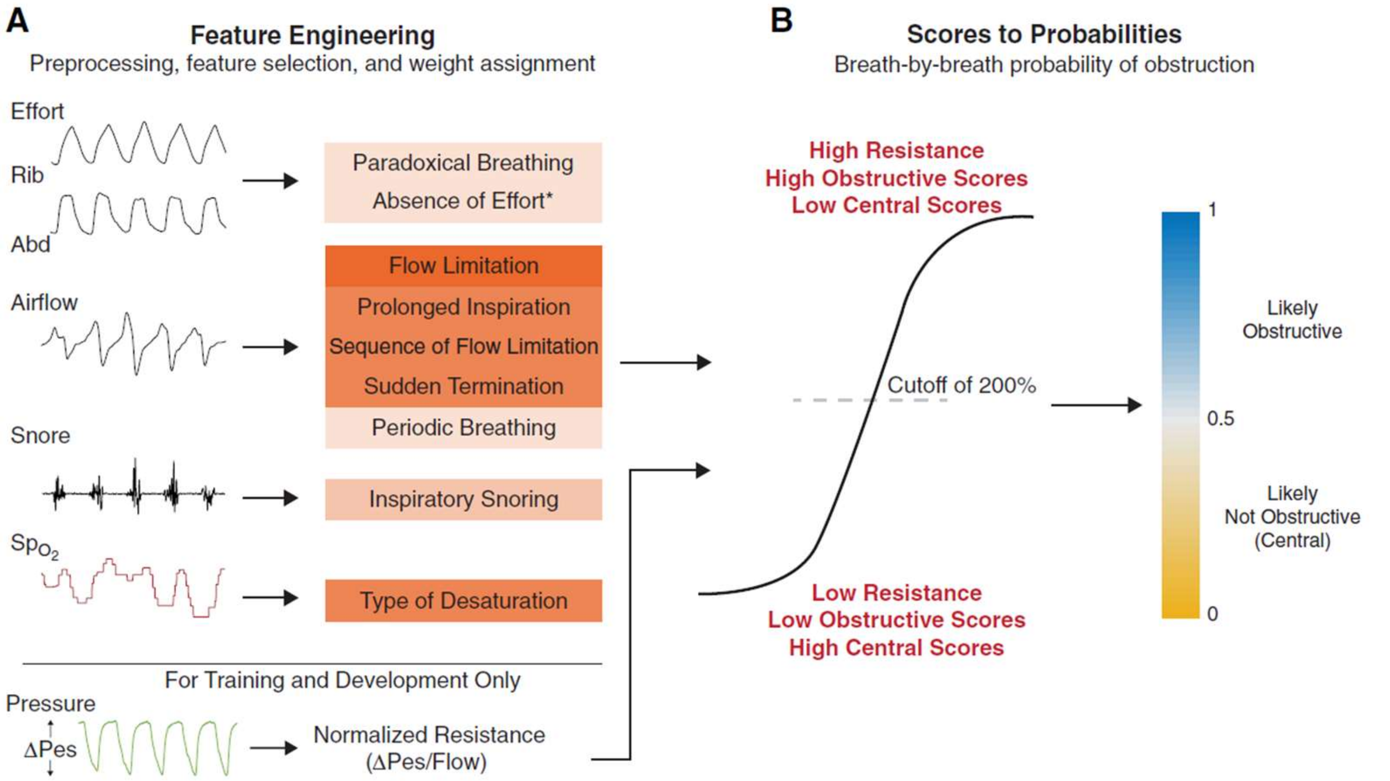


SAO2 (%)
100
80
VTH (uV)
-99
-299
VAB (uV)
-99
-299
NAF1 (uV)
50
-50
NAF2P (-)
25
-25
PR (BPM)
101
21
PTT (ms)
392
367
ECG (mV)
-- Hz
2.0
-- Hz
PULSE (uV)
-- Hz
1000
-- Hz
135 s
N1 N2 N2 N2 N2 N2 N2 N2 N2 N2 N2 N2 W N2 N2 N1 N2 N2 N2 N2 N2
2.0 m
PneuSD
uV
Hz
TC
50Hz
9 Ch.
NA PNEUM
+07:39:00


N2
N2
N2
N2
N2
N2
N2
N2
N2
N2
N2
245 s
N1
N2
N2
N2
N2
N2
N2
N2
N2
N2
N2
N2
W
N2
N2
N1
N2
N2
N2

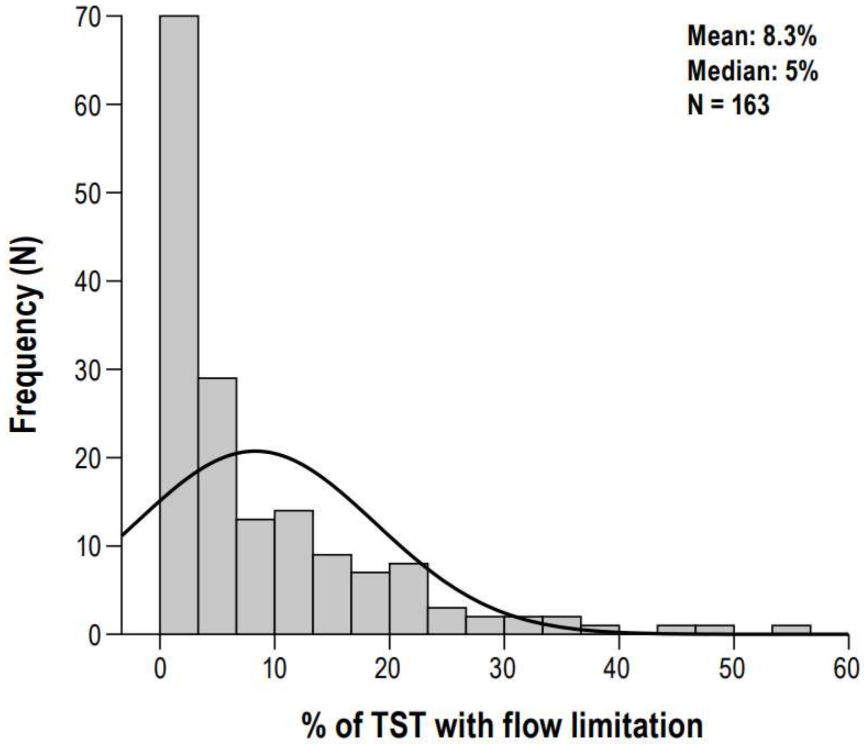
Endotyping Sleep Apnea One Breath at a Time
An Automated Approach for Separating Obstructive from Central Sleep-disordered Breathing

American Journal of Respiratory and Critical Care Medicine Volume 204 Number 12 | December 15 2021

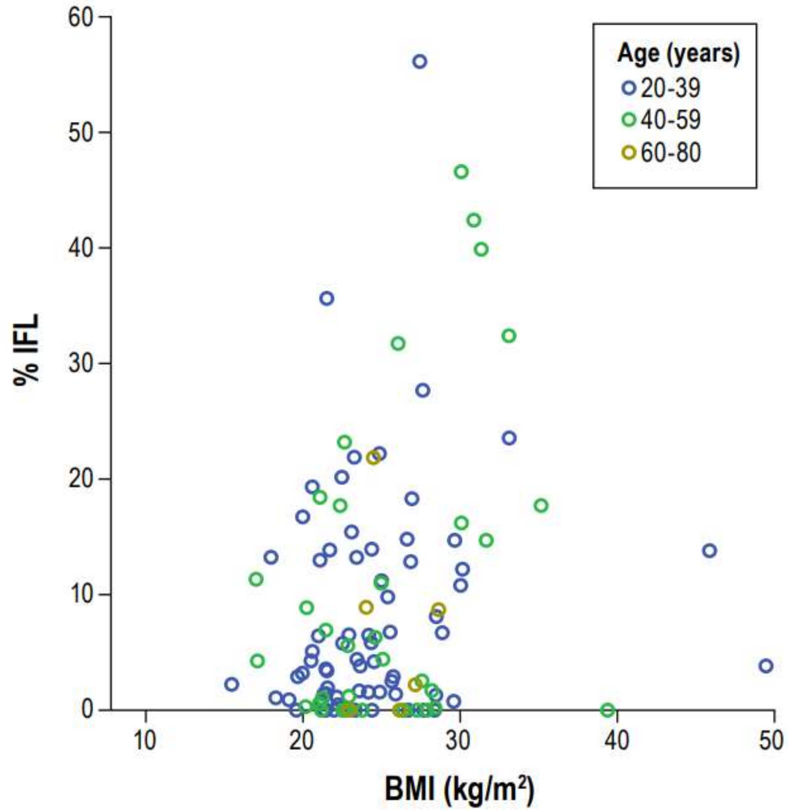


Inspiratory Flow Limitation in a Normal Population of Adults in São Paulo, Brazil

Distribution of inspiratory flow limitation in the normal group.



Correlation between percentage of total sleep time with inspiratory flow limitation (IFL) and body mass index (BMI) according to age groups



Palombini et al. *SLEEP* 2013

Inspiratory Flow Limitation in a Normal Population of Adults in São Paulo, Brazil

	Unstandardized Coefficients B	Std. Error	Standardized Coefficients Beta	Sig.
1 (Constant)	-145.596	119.616		0.229
BMI	0.686	0.309	0.315	0.031
Age	-0.040	0.149	-0.048	0.788
Arousal index	0.138	0.205	0.112	0.505
Sleep efficiency	-0.020	0.173	-0.023	0.909
PLM index	1.293	1.057	0.178	0.227
SWS	0.215	0.233	0.159	0.361
Stage REM	0.021	0.291	0.012	0.943
AHI	-0.553	1.115	-0.068	0.622
Desaturation index	-0.311	0.520	-0.078	0.553
% time SpO_2 < 90%	-0.237	0.481	-0.066	0.624
Lowest SpO_2	1.113	1.051	0.174	0.295
Mean SpO_2	0.331	1.418	0.037	0.816

Regression model for inspiratory flow limitation and anthropomorphic and PSG variables

AHI, apnea-hypopnea index; BMI, body mass index; PLM, periodic limb movement; REM, rapid eye movement; SpO2, oxyhemoglobin saturation; SWS, slow wave sleep.

Palombini et al. *SLEEP* 2013

UARS: patients have worse sleep quality compared to mild OSA

Table 1. Descriptive data.

Descriptive variables	Control (n = 34)	UARS (n = 34)	Mild OSA (n = 47)	F	Effect size	Observed power
Gender (M/F)	15/19	14/20	21/26	-	-	-
Age (years)	36.76±8.99	42.91±8.0*	46.67±9.37**	12.16	0.18	0.99
BMI (kg/m^2)	24.40±3.12	25.94±3.94	28.28±3.41**[£]	12.43	0.18	0.99
Schooling years	16.20±4.16	13.76±3.93*	13.59±3.31**	5.42	0.09	0.84

* $p < 0.05$ between control group and UARS
** $p < 0.05$ between control group and Mild OSA
[£] $p < 0.05$ UARS group and Mild OSA
Data represented by Mean ± Standard deviation and 95% Confidence Interval (lower and upper); General Linear Model (GLM)

De Godoy et al PLoS ONE 2016; 11(5): e0156244.

Upper Airway Resistance Syndrome Patients Have Worse Sleep Quality Compared to Mild Obstructive Sleep Apnea

Table 2. Questionnaires.

Questionnaires	Control (n = 34)		UARS (n = 34)		Mild OSA (n = 47)	
	Mean ± SD	95% CI	Mean ± SD	95% CI	Mean ± SD	95% CI
Epworth	6.43±2.9	5.39–7.48	12.70 ±4.37*	11.10–14.31	12.45±4.82**	11.02–13.89
Fatigue	27.83±16.23	21.42–33.13	47.38±17.42*	40.99–53.77	44.15±16.88**£	39.13–49.16
Pittsburg 1	1.21±0.65	0.98–1.45	1.93±1.06*	1.54–2.32	1.73±0.61	1.55–1.92
Pittsburg 2	0.90±0.77	0.62–1.18	1.35±1.14	0.93–1.77	1.26±0.95	0.97–1.54
Pittsburg 3	1.25±0.80	0.96–1.53	1.54±0.92	1.20–1.88	1.47±0.88	1.21–1.74
Pittsburg 4	0.68±0.99	0.32–1.04	0.74±0.96	0.38–1.09	1.00±1.13	0.66–1.33
Pittsburg 5	1.18±0.69	0.93–1.43	1.83±0.68	1.58–2.09	1.78±0.59	1.60–1.95
Pittsburg 6	0.12±0.42	(-0.02)-0.27	1.77±0.76*	1.49–2.05	0.36±0.92**£	0.09–0.64
Pittsburg 7	0.75±0.84	0.44–1.05	1.09±1.01	0.72–1.46	1.47±0.80**	1.23–1.71
Pittsburg Total	6.12±2.99	5.04–7.20	10.61±4.81*	8.84–12.37	9.10±3.02**£	8.21–10.00
FOSQ General productivity	3.52±0.45	3.35–3.68	2.83±0.81*	2.53–3.13	3.22±0.55£	3.05–3.39
FOSQ Social outcome	3.70±0.48	3.35–4.12	2.95±1.01*	2.58–3.32	3.32±0.78£	3.09–3.55
FOSQ Activity level	3.35±0.46	3.18–3.51	2.72±0.85*	2.42–3.02	3.01±0.59£	2.84–3.18
FOSQ Vigilance	3.46±0.53	3.27–3.65	2.71±0.85*	2.39–3.02	3.03±0.66£	2.83–3.22
FOSQ Intimate Relationshipsd and Sexual Activity	3.34±0.81	3.04–3.63	2.71±1.21	2.27–3.16	3.17±0.86£	2.92–3.43
FOSQ Total	17.28±2.29	16.46–18.11	13.50±3.65*	12.16–14.84	15.42±3.08£	14.50–16.33
BECK Anxiety	7.65±8.50	4.58–10.72	19.22±14.41*	13.93–24.51	13.82±11.88£	10.29–17.35
BECK Depression	8.18±5.69	6.13–10.24	17.48±10.84*	13.50–21.46	13.10±6.96**£	11.03–15.17

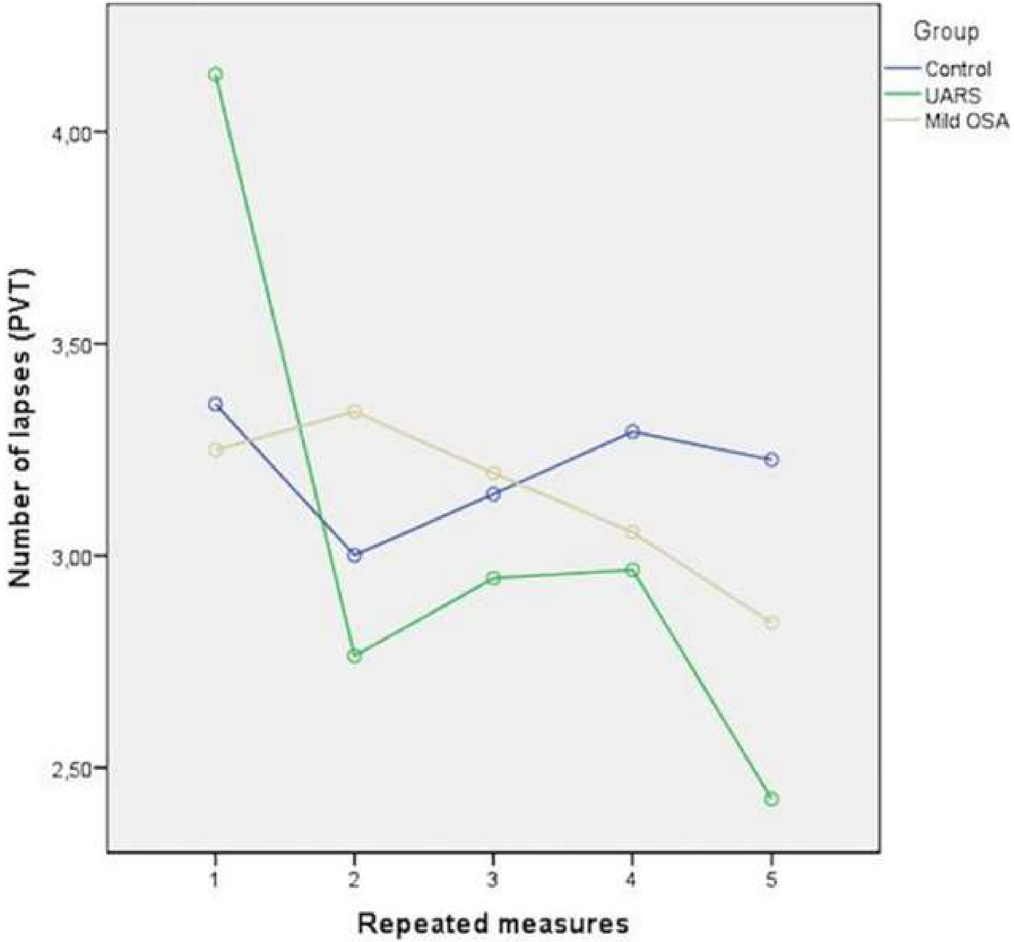
* $p < 0.05$ between control group and UARS

** $p < 0.05$ between control group and Mild OSA

£ $p < 0.05$ UARS group and Mild OSA

Data represented by Mean ± Standard deviation and 95% Confidence Interval (lower and upper); Generalized Linear Model (GLzMM)

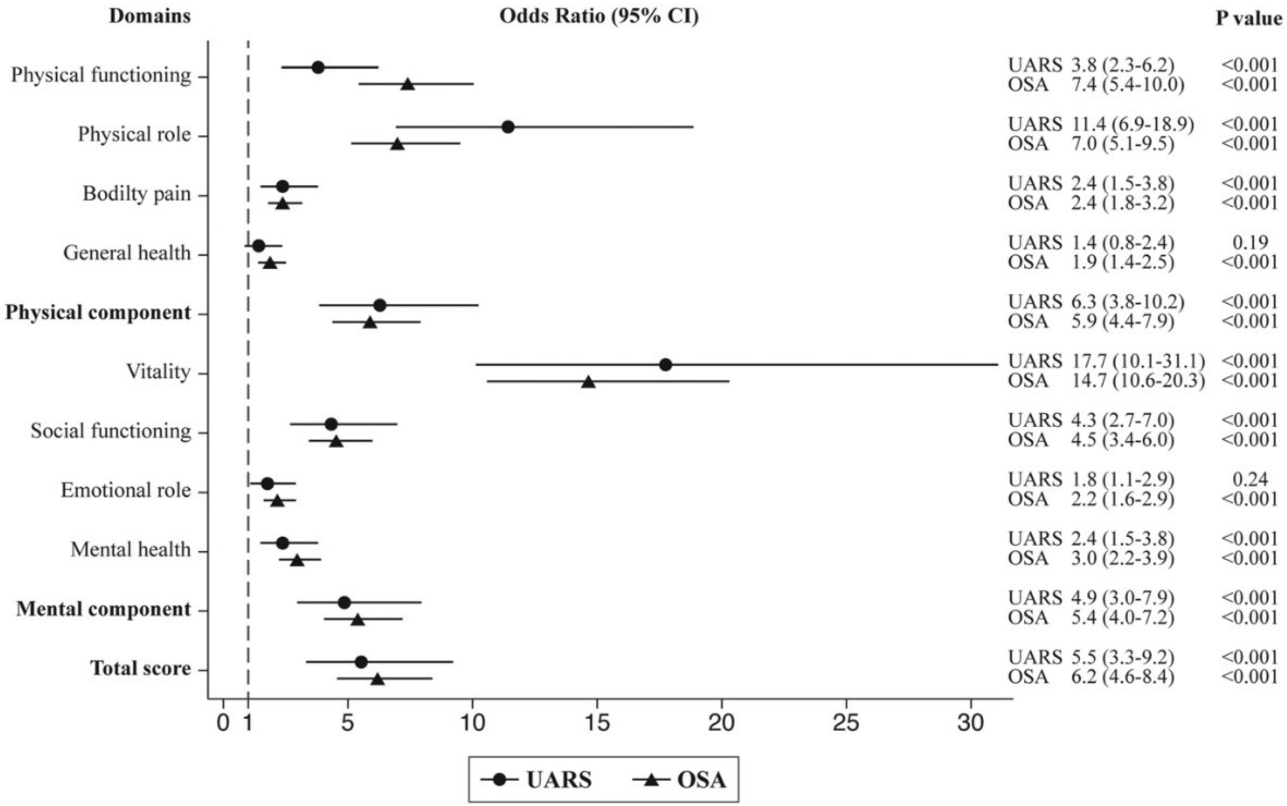
Upper Airway Resistance Syndrome Patients Have Worse Sleep Quality Compared to Mild Obstructive Sleep Apnea



Number of lapses of PVT repeated measures: mild OSA patients had more lapses at times 2 than at time 5 than "control group" ($p = 0.044$). UARS patients had more lapses at time 1 than at time 5 in comparison to mild OSA patients ($p = 0.02$).

De Godoy. et al. *PLoS ONE* 2016

Risk of low score in HRQoL in patients with UARS and patients with OSA compared to participants in the GP



Odds ratios adjusted for age and sex. The city and socioeconomic status were the same for the GP data and UARS and OSA data. CI = confidence interval, GP =general population, HRQoL = health-related quality of life, OSA = obstructive sleep apnea, UARS = upper airway resistance syndrome.

Vizcarra-Escobar D. et al. *JCSM* 2022

The role of mean inspiratory effort on daytime sleepiness

Z. Pelin, Eur Respir J 2003; 21: 688–694

Table 4. – Correlation coefficients and their significance for Epworth and multiple sleep latency test (MSLT) scores in upper airway resistance syndrome (UARS) and obstructive sleep apnoea syndrome (OSAS) patients

	UARS		OSAS	
	r	p-value	r	p-value
Epworth score				
Arousal index	0.20	0.24	0.31	0.04
RDI	0.20	0.24	0.33	0.03
Average *P*oes	0.48	0.03	0.44	0.01
Δ*P*oes	0.31	0.12	0.34	0.02
Stage variations n	-0.19	0.47	0.26	0.07
Min. O_2 %	-0.28	0.15	-0.18	0.15
%TST with O_2 <90%			0.26	0.07
MSLT score				
Arousal index	-0.26	0.46	-0.16	0.18
RDI	-0.01	0.49	-0.14	0.22
Average *P*oes	-0.35	0.10	0.02	0.45
Δ*P*oes	-0.22	0.21	0.06	0.36
Stage variations n	0.28	0.16	0.13	0.23
Min. O_2 %	0.38	0.09	0.23	0.1
% TST with O_2 <90%			-0.13	0.24

RDI: respiratory disturbance index; *P*oes: oesophageal pressure; Min.: minimum; O_2: oxygen; TST: total sleep time.

ERS

INTERNATIONAL CONGRESS 2022

Percentage of sleep time with increase in respiratory effort is a strong predictor of prevalent hypertension in OSA patients

Jean-Benoit Martinot[1,2], Nhat-Nam Le-Dong[3], Atul Malhotra[4] and Jean-Louis Pépin[5]

[1]Sleep Laboratory, CHU Université Catholique de Louvain (UCL) Namur Site Sainte-Elisabeth, Namur, Belgium

[2]Institute of Experimental and Clinical Research, UCL Bruxelles Woluwe, Brussels, Belgium

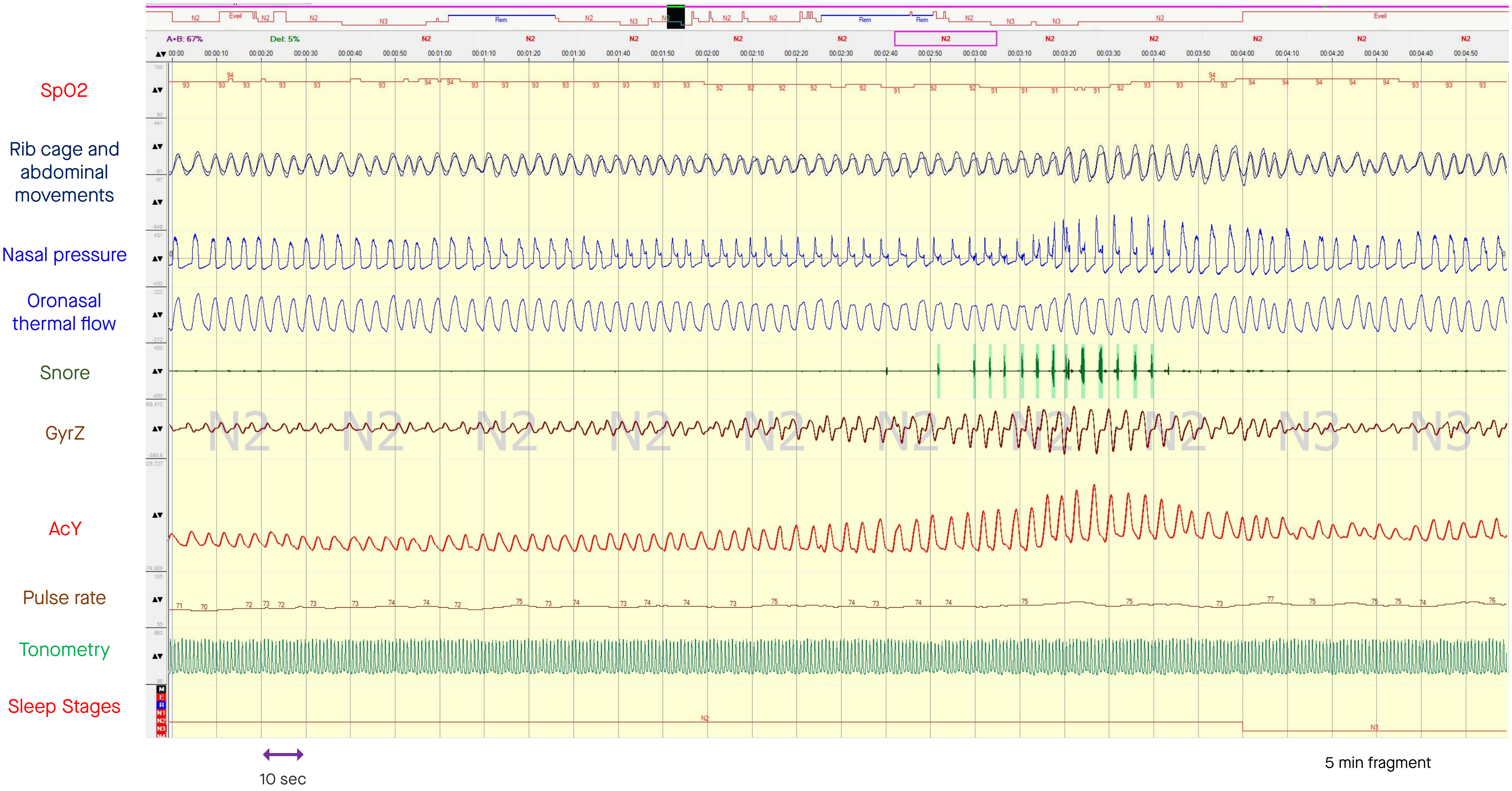
[3]Sunrise, Namur, Belgium

[4]University of California San Diego, La Jolla, CA, USA

[5]HP2 Laboratory, Inserm U1300, University Grenoble Alpes, Grenoble, France

CHU UCL NAMUR

UGA Université Grenoble Alpes



SpO2
Rib cage and abdominal movements
Nasal pressure
Oronasal thermal flow
Snore
GyrZ
AcY
Pulse rate
Tonometry
Sleep Stages
10 sec
5 min fragment

Phenotypes du Syndrome de Haute Resistance des VRS

- Jeune adulte maigre au sommeil non rafraichissant exposé à une pression de sommeil la journée mais aussi à une variété de plaintes peu spécifiques somatiques ou psychosomatiques voire de manifestations plus psychiatriques (inattention, hyperactivité, anxiété , dépression) à une insomnie

et/ ou à de la fatigue chronique

- montrant des troubles de croissance cranio faciale ou /et dento-squeletique
- Jeune adulte ou d' âge moyen en net surpoids voire obése
- Jeune adulte exposé a une allergie nasale mal contrôlée
- Hypersomnie avec allongement du temps de sommeil
- Ronflement non apnéique Primary Snoring
- Lipothymie de la consultation cardiologique
- La femme pendant la grossesse ou au décours de la ménopause