

Effets métaboliques des troubles respiratoires du sommeil

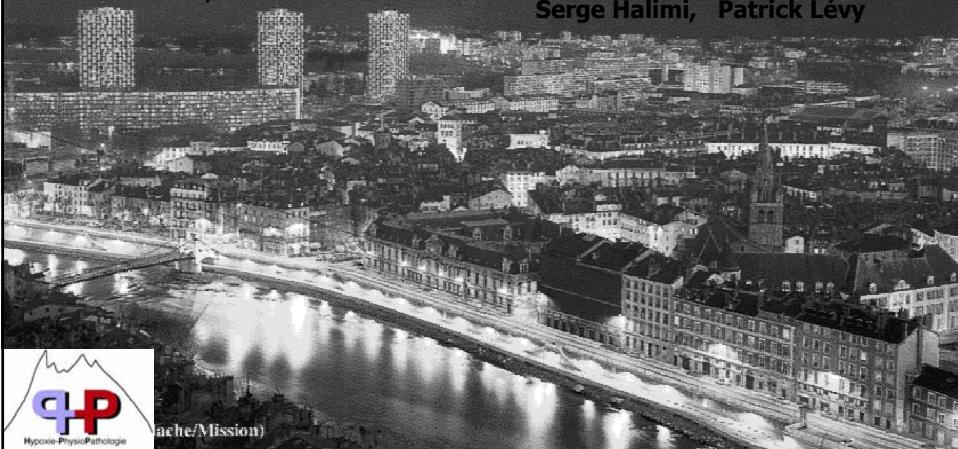
Laboratoire du sommeil Grenoble

Jean Louis Pépin, Pierre-Yves Benhamou

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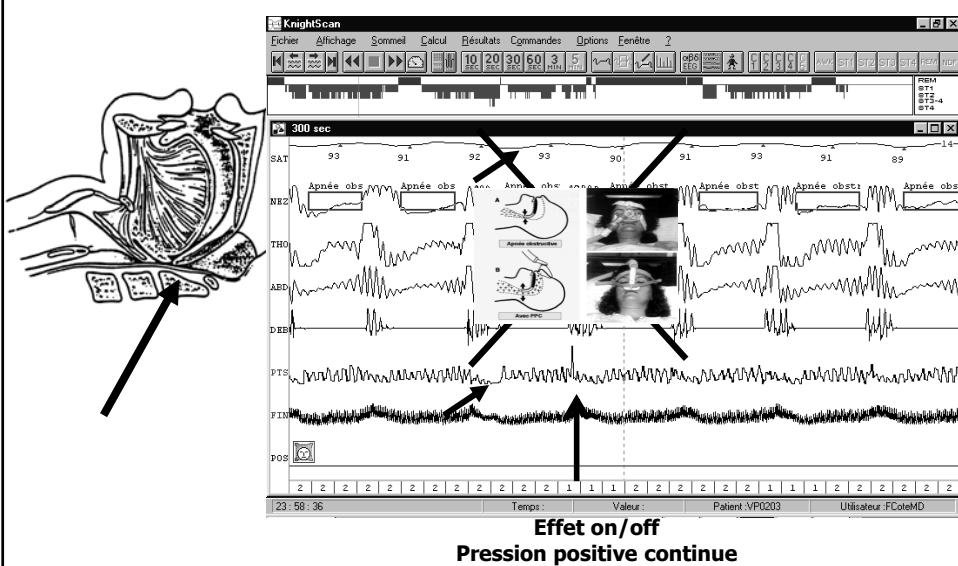
Anne Laure Borel, Renaud Tamisier ,

Serge Halimi, Patrick Lévy

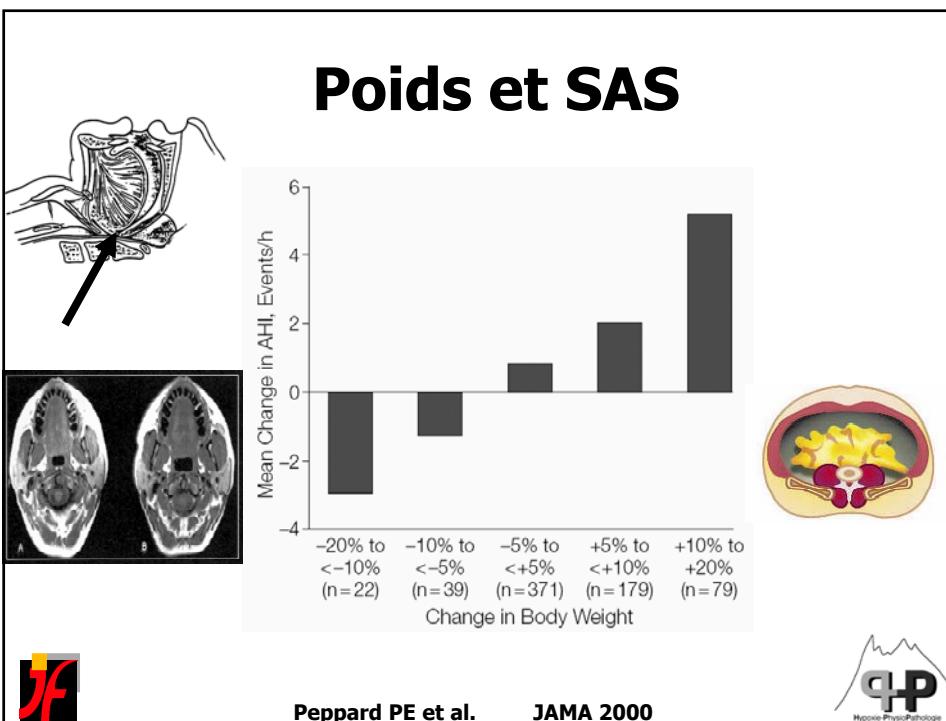
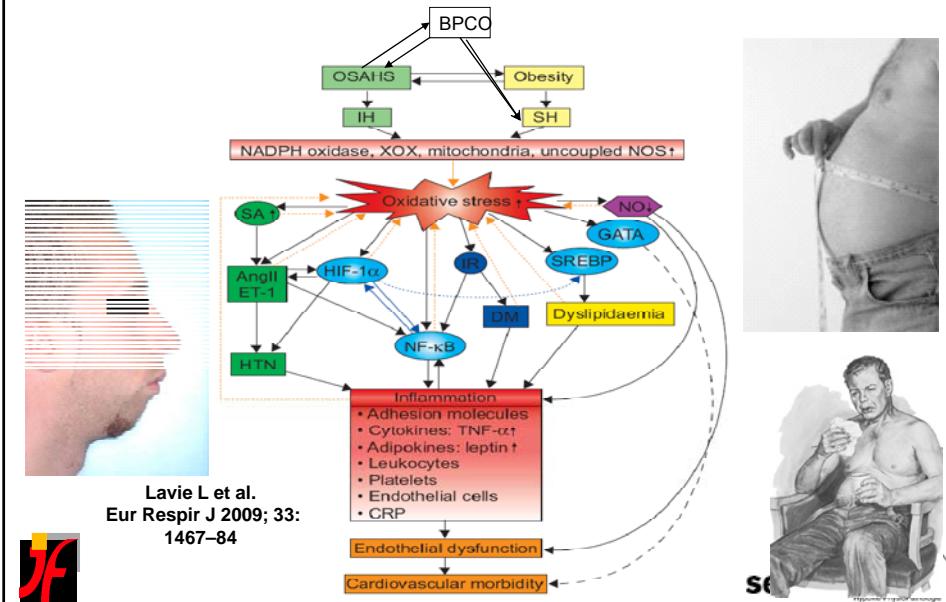


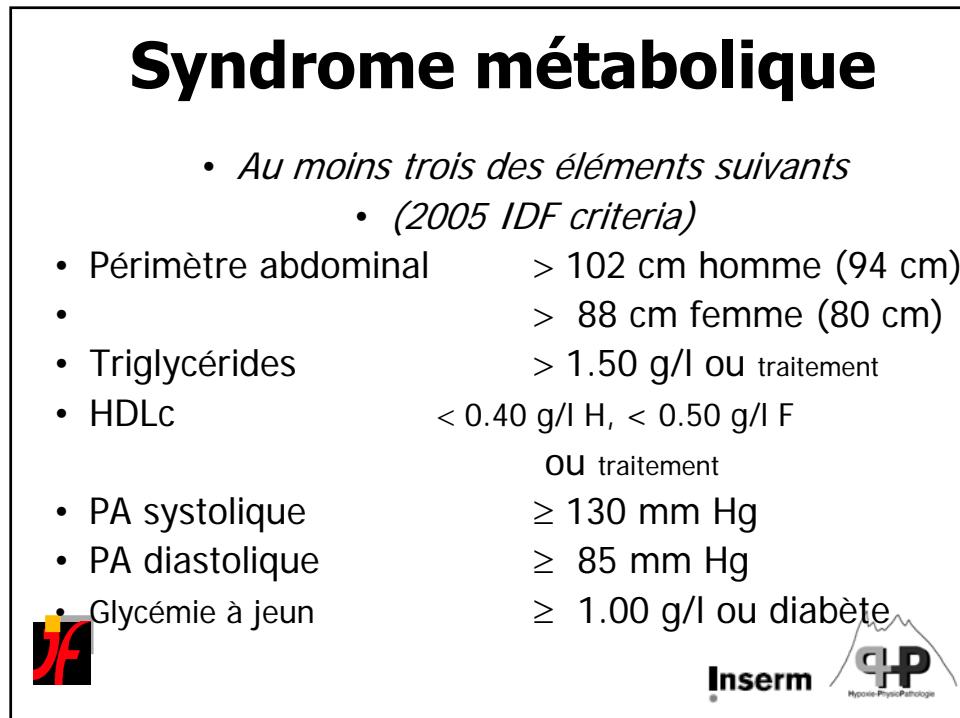
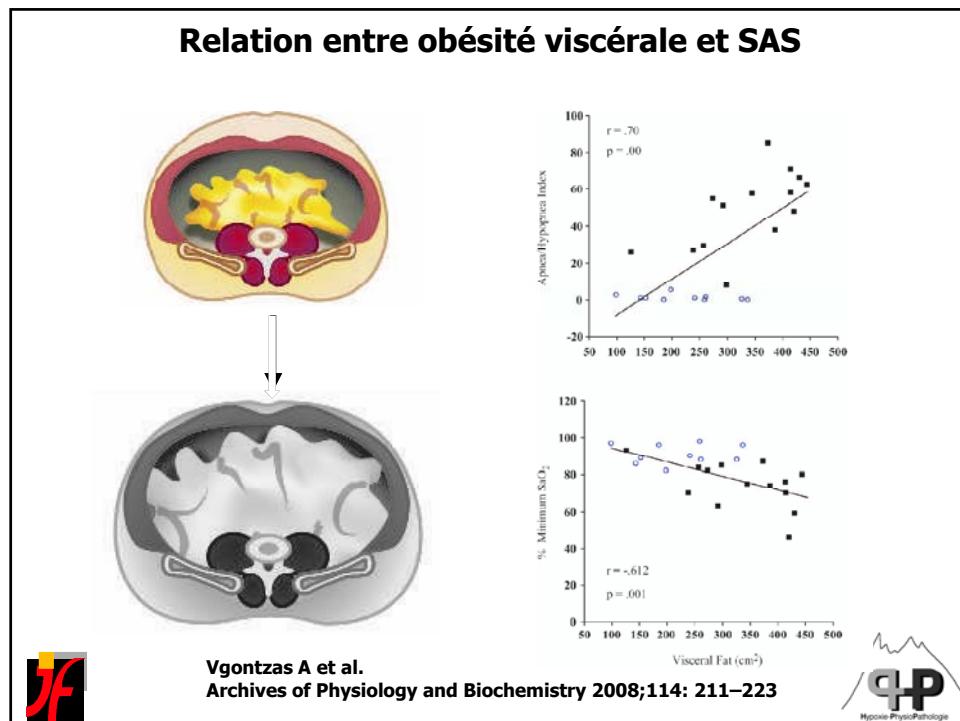
Syndrome d'apnées du sommeil

Hypoxie intermittente et fragmentation du sommeil

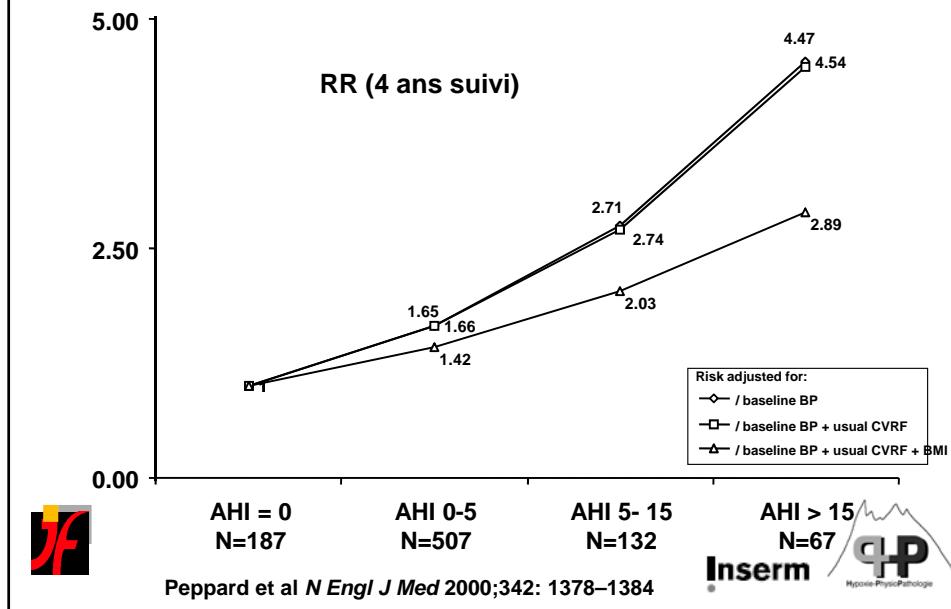


Syndrome d'apnées du sommeil obstructif : différents phénotypes





Effet dose réponse entre SAS et PA

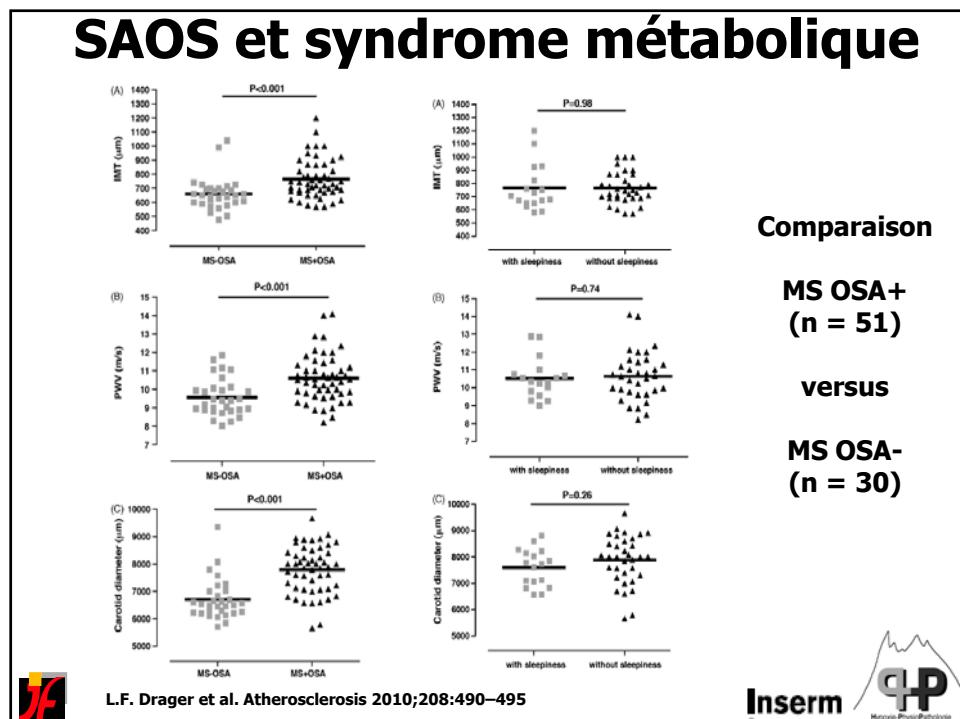
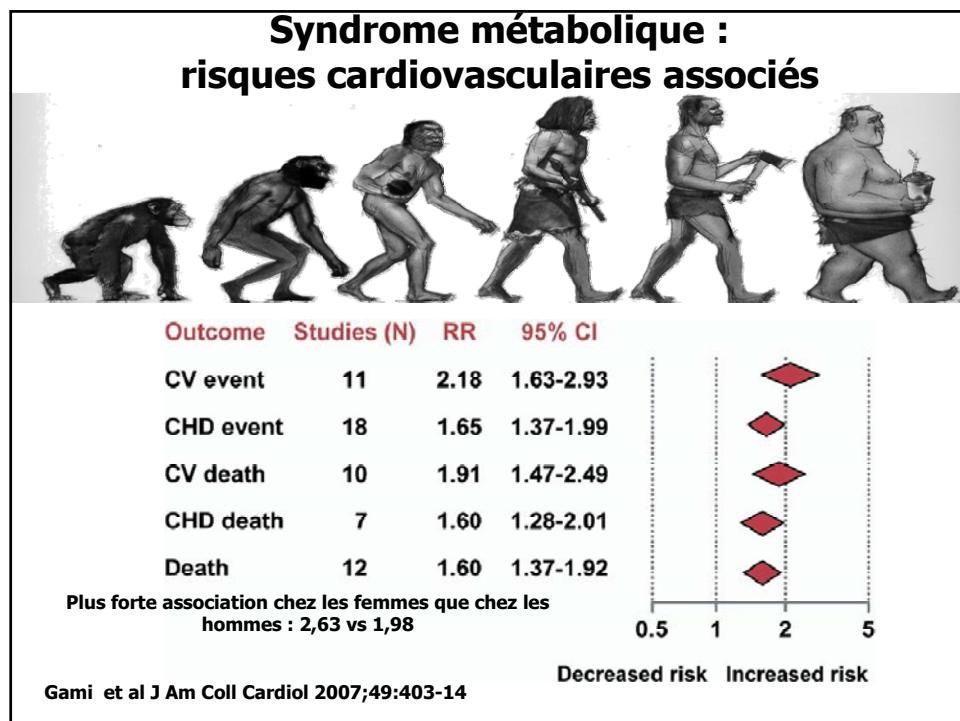


SAOS et syndrome métabolique

Reference	Design	Study Population	Main Results
Coughlin and colleagues (8)	Case controlled (matched for BMI) OSA: AHI > 15 Control subjects: AHI < 5 MS: NCEP (ATP III) criteria	All men 61 OSA 43 Control subjects	Independent* associations between: 1. OSA and MS (OR, 9.1) 2. OSA and systolic and diastolic blood pressure, fasting insulin, triglyceride, HDL cholesterol, total/HDL cholesterol
Gruber and colleagues (9)	Case controlled OSA: AHI criteria not given MS: International Diabetes Federation criteria	38 OSA 41 Control subjects	Independent* association between: 1. OSA and MS (OR, 5.9) 2. No independent association between OSA and insulin resistance (assessed by HOMA)
Lam and colleagues (10)	Community based Full PSG OSA: AHI ≥ 5 MS: NCEP (ATP III) criteria [†]	Chinese 30-65 yr old 255 Subjects (150 men and 105 women)	OSA and MS (OR, 5.3) Independent association between OSA and waist, diastolic blood pressure*, fasting glucose*, MS* Independent determinants of OSA: age, gender, BMI, MS
Sasanabe and colleagues (11)	Sleep clinic and community volunteers Full PSG OSA: AHI ≥ 15 Control subjects: AHI < 5 MS: criteria for Japanese population	Japanese 819 OSA (719 men and 100 women) 89 Control subjects	Independent* association between OSA and MS in men, but not in women
Parish and colleagues (13)	Retrospective PSG and chart review	228 Consecutive patients 146 OSA 82 No OSA	Higher prevalence of MS in patients with OSA (60 vs. 40%)
Coughlin and colleagues (12)	Randomized, controlled crossover study CPAP vs sham CPAP MS: NCEP (ATP III) criteria	34 Men Mean AHI = 40 Mean BMI = 36 Mean age = 49 yr	No change in proportion of subjects with MS with CPAP treatment Significant decrease in blood pressure

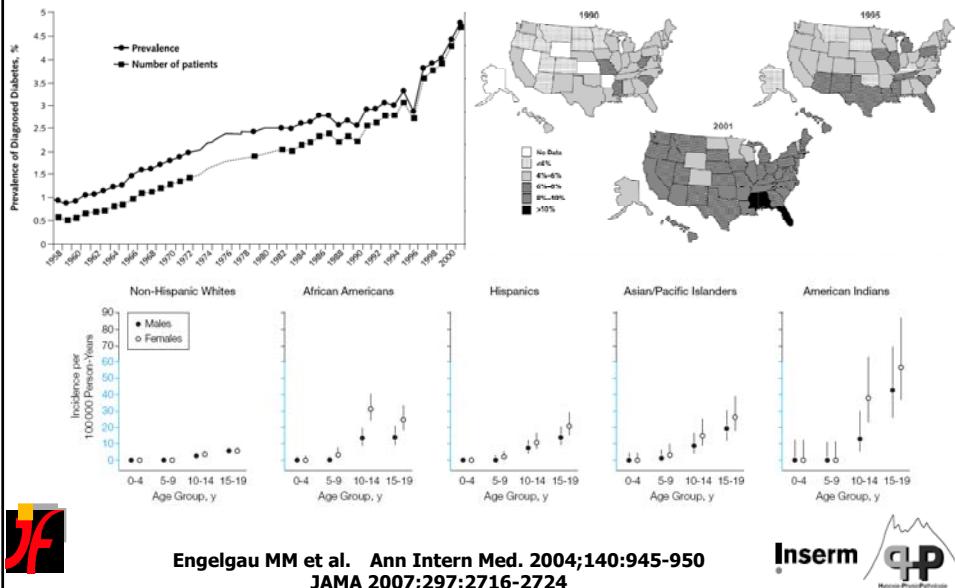
Tasali E and Ip M. PATS 2008;5:207–217

JF Inserm Hypoxie-Physiopathologie



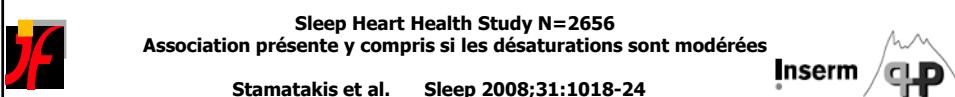
Syndrome d'apnées du sommeil et diabète

Le diabète type 2 une situation de pandémie !



Syndrome d'apnées du sommeil et diabète

AHI (ΔSaO_2 criteria)	AHI cut points (events/hr)	Impaired fasting glucose (%)	Diabetic fasting glucose (%)	Adjusted cumulative odds ratio (95% CI) ^a
AHI ($\Delta SaO_2 \geq 4.0\%$)				Reference
Model 1				
I	<1.44	22.6	4.4	1.06 (0.82–1.37)
II	1.44–4.60	31.5	3.5	1.32 (1.02–1.71)
III	4.61–11.37	35.5	7.1	1.35 (1.04–1.76)
IV	≥11.38	42.0	8.3	
AHI ($\Delta SaO_2 \geq 3.0\%–3.9\%$)				
Model 2				
I	<2.25	21.8	3.2	Reference
II	2.25–4.37	32.3	5.3	1.53 (1.13–2.06)
III	4.38–7.33	35.2	6.3	1.53 (1.10–2.15)
IV	≥7.34	42.2	8.4	1.72 (1.20–2.48)
AHI ($\Delta SaO_2 \geq 2.0\%–2.9\%$)				
Model 3				
I	<4.69	25.4	3.8	Reference
II	4.69–7.27	30.0	4.5	0.93 (0.71–1.20)
III	7.27–10.92	34.2	6.2	1.18 (0.90–1.54)
IV	≥10.93	42.0	8.7	1.41 (1.07–1.86)
AHI ($\Delta SaO_2 \geq 0.0\%–1.9\%$)				
Model 4				
I	<5.48	33.2	5.0	Reference
II	5.48–9.04	33.3	5.3	1.00 (0.79–1.27)
III	9.04–14.69	31.3	6.5	1.06 (0.83–1.34)
IV	≥14.70	33.8	6.5	1.07 (0.84–1.37)



Syndrome d'apnées du sommeil et diabète

Unadjusted model		Adjusted for age and gender		Multivariate adjusted model*	
OR (95% CI)	p Value	OR (95% CI)	p Value	OR (95% CI)	p Value
Definition: Diabetes (self-report + medications)					
Mild OSA	1.25 (0.71 to 2.18)	0.44	1.21 (0.69 to 2.13)	0.51	0.95 (0.53 to 1.71) 0.86
Moderate OSA	1.75 (0.98 to 3.13)	0.059	1.65 (0.91 to 2.97)	0.10	1.02 (0.54 to 1.93) 0.94
Severe OSA	3.93 (2.34 to 6.58)	<0.001	3.79 (2.23 to 6.45)	<0.001	2.18 (1.22 to 3.89) 0.008
Test for trend		<0.001		<0.001	0.005
Definition: Diabetes administrative algorithm (two physician claims or one hospitalisation within a 2-year period)					
Mild OSA	1.25 (0.79 to 1.98)	0.34	1.14 (0.72 to 1.82)	0.58	0.90 (0.53 to 1.53) 0.70
Moderate OSA	1.46 (0.89 to 2.38)	0.14	1.26 (0.76 to 2.09)	0.36	0.88 (0.49 to 1.58) 0.68
Severe OSA	3.63 (2.36 to 5.58)	<0.001	3.18 (2.04 to 4.95)	<0.001	1.82 (1.07 to 3.10) 0.027
Test for trend		<0.001		<0.001	0.035
Sleepy (ESS ≥10)			Non-sleepy (ESS <10)		
OR (95% CI)	p Value	OR (95% CI)	p Value	OR (95% CI)	p Value
Unadjusted model					
Mild OSA	1.24 (0.65 to 2.38)	0.51	1.47 (0.47 to 4.60)	0.51	
Moderate OSA	1.70 (0.87 to 3.32)	0.12	2.03 (0.61 to 6.76)	0.25	
Severe OSA	4.11 (2.30 to 7.33)	<0.001	2.79 (0.87 to 9.00)	0.09	
Multivariate adjusted model*					
Mild OSA	0.98 (0.50 to 1.94)	0.96	0.94 (0.28 to 3.17)	0.92	
Moderate OSA	1.13 (0.54 to 2.32)	0.75	0.820.21 to 3.14)	0.77	
Severe OSA	2.59 (1.35 to 4.97)	0.004	1.16 (0.31 to 4.37)	0.83	

SAS associé au diabète de type 2 après ajustement données anthropométriques, poids, tour cou.
Ceci n'est vrai que chez les somnoles

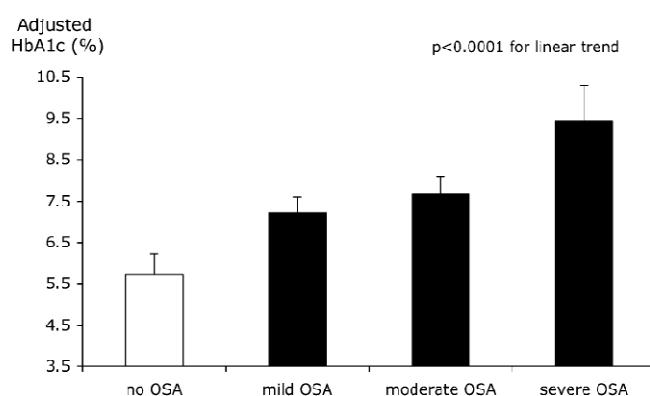


Cohorte observationnelle CANADA N=2149

Ronsley PE et al. Thorax 2009;64:834-39



Syndrome d'apnées du sommeil et diabète Relation proportionnelle entre sévérité du SAS et contrôle du diabète



60 diabètes de type 2 consécutifs

Ajusté pour âge, sexe, race, IMC, Traitements médicamenteux du diabète, quantité exercice physique, ancienneté du diabète, TST polysomnographie.

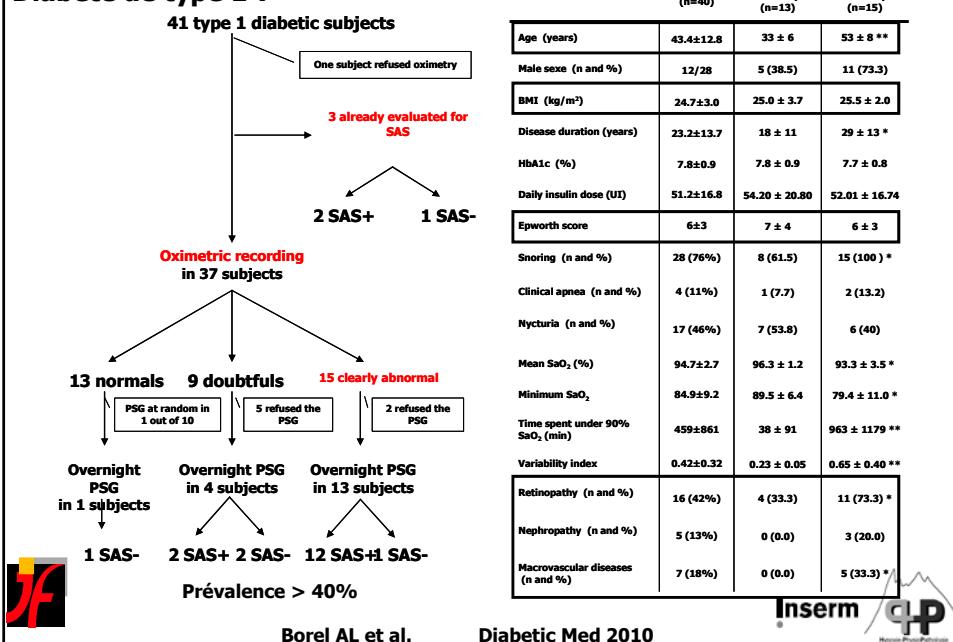


Aronsohn A et al. Am J Respir Crit Care 2010;181:507-513

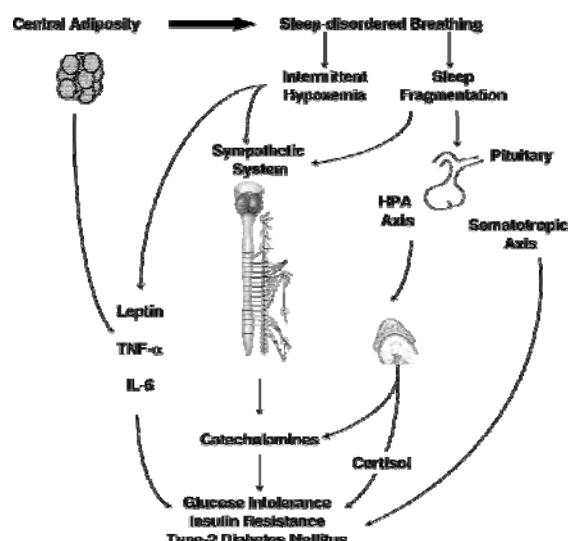


Syndrome d'apnées du sommeil et diabète

Diabète de type 1 ?



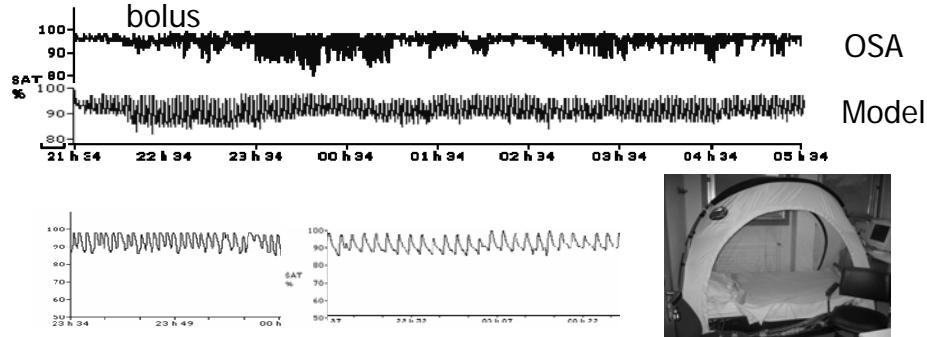
Syndrome d'apnées du sommeil et diabète



Inserm **CP** Centre de Pédiatrie

Hypoxie intermittente chez le sujet normal

Model: Oxygen fraction reduced to 12%, oxygen bolus



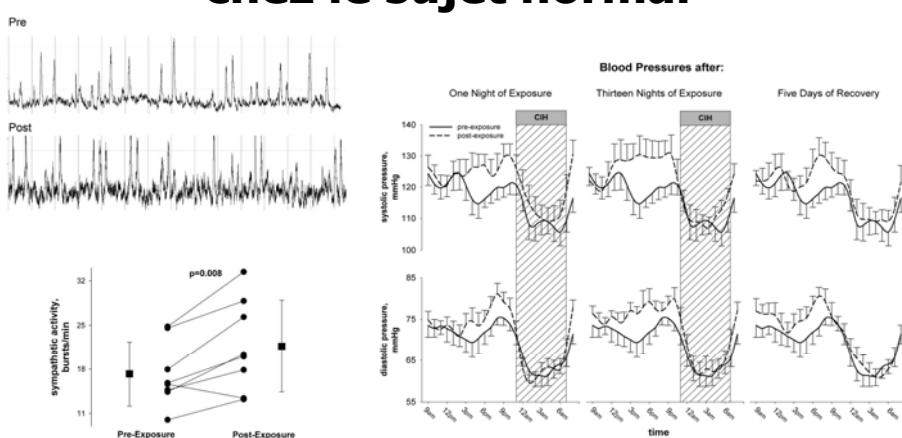
	Pre exp.	1 st night	14 th night
ODI / h	0.4 ± 0.9	37.2 ± 7.7 *	35.4 ± 7.5 *
Micro-arousals / h	19.6 ± 9.5	36.6 ± 10.9*	33.9 ± 9.4 *

Tamisier et al. J Appl Physiol 2009

Weiss et al. Sleep Med 2009

Recherche collaborative JW Weiss, Harvard MS, Boston

Hypoxie intermittente chez le sujet normal

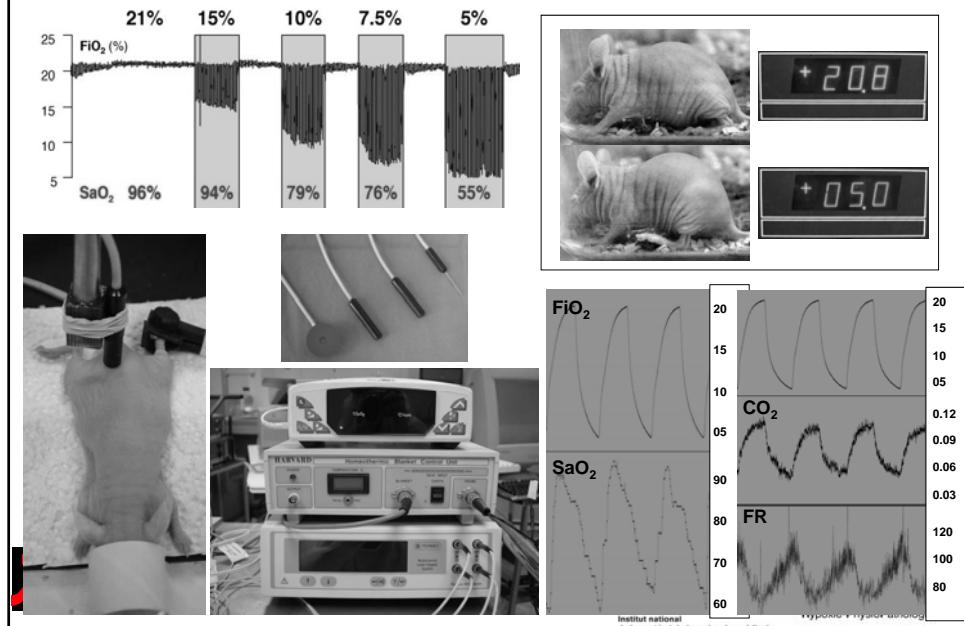


Tamisier et al. Eur Resp J 2011

Gilmartin et al. Am J Physiol 2010

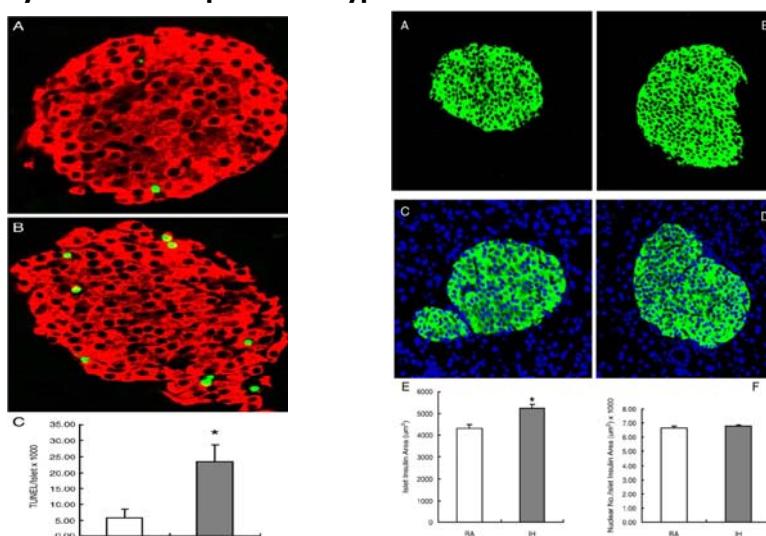
Recherche collaborative JA Taylor et JW Weiss, Harvard MS, Boston

Modèles animaux



Syndrome d'apnées du sommeil et diabète

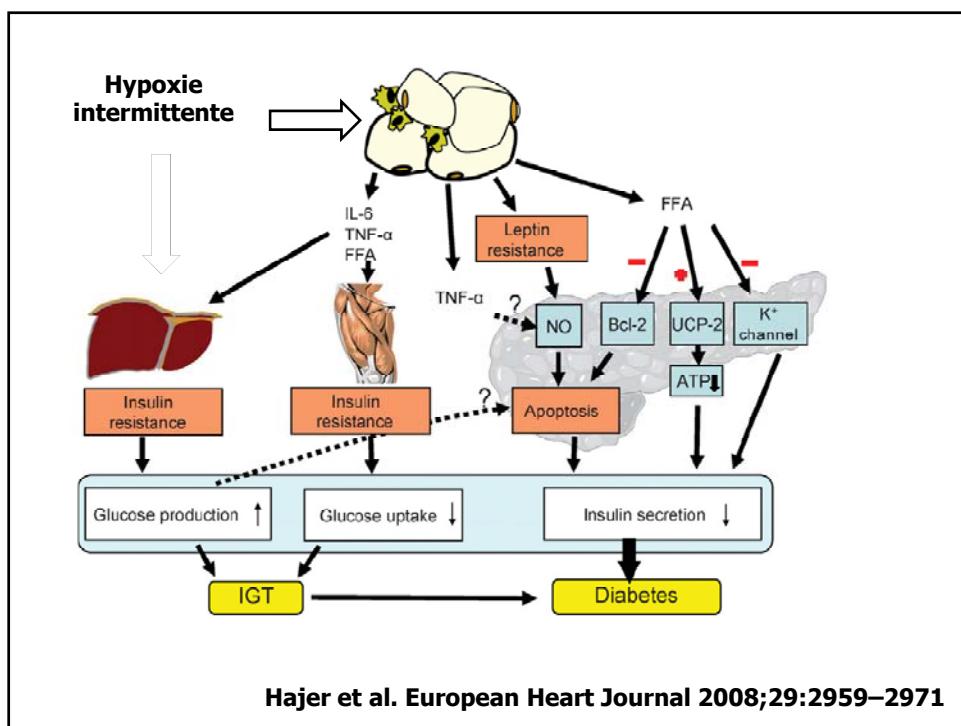
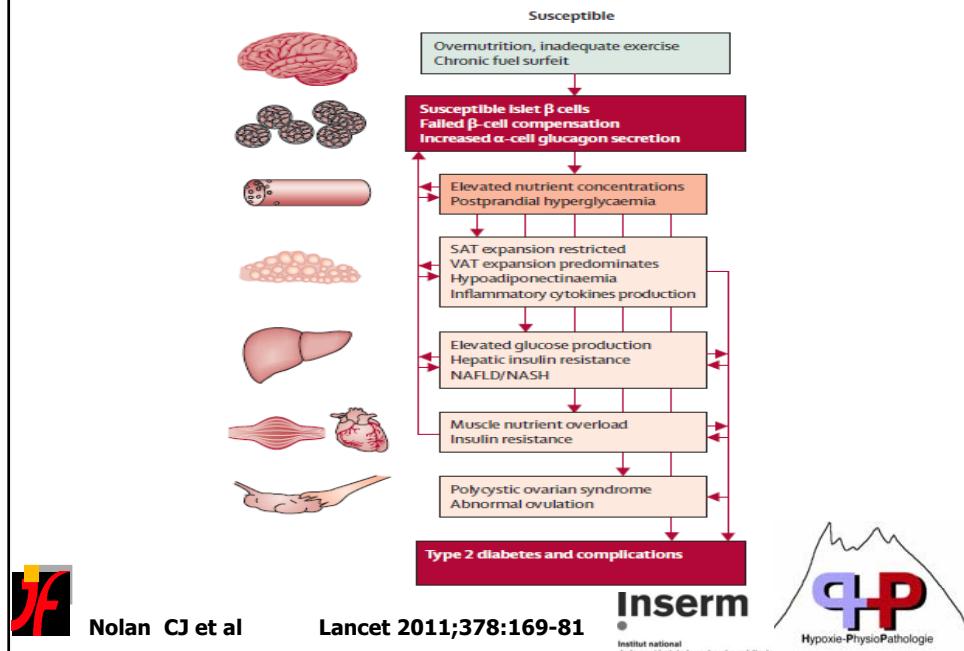
Cellules Beta : Mort cellulaire et prolifération augmentées en rapport avec le stress oxydant souris exposées à l'hypoxie intermittente



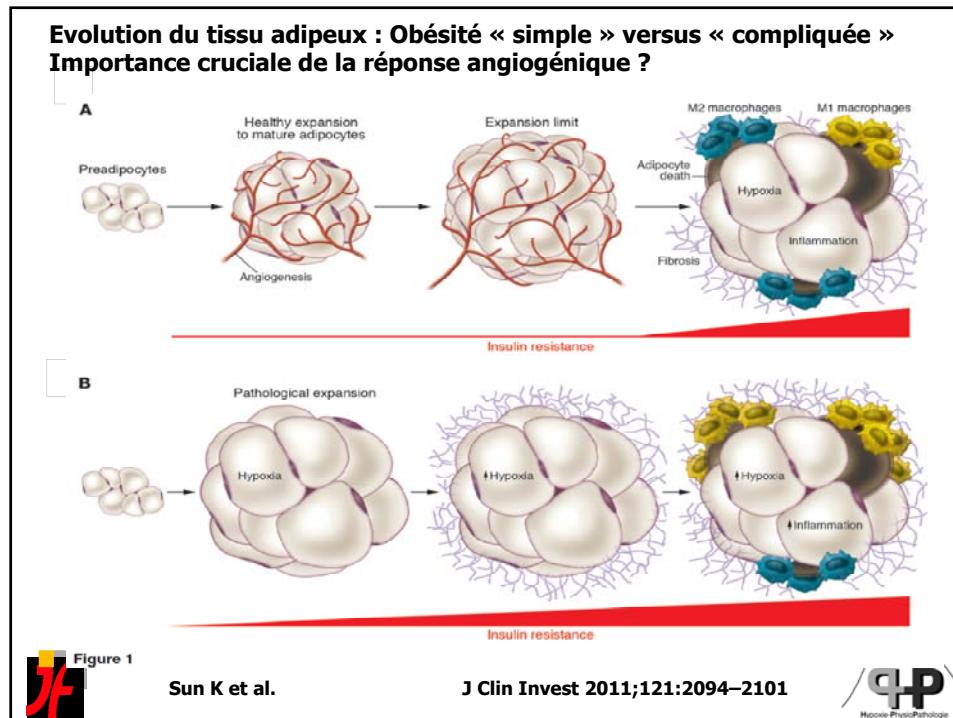
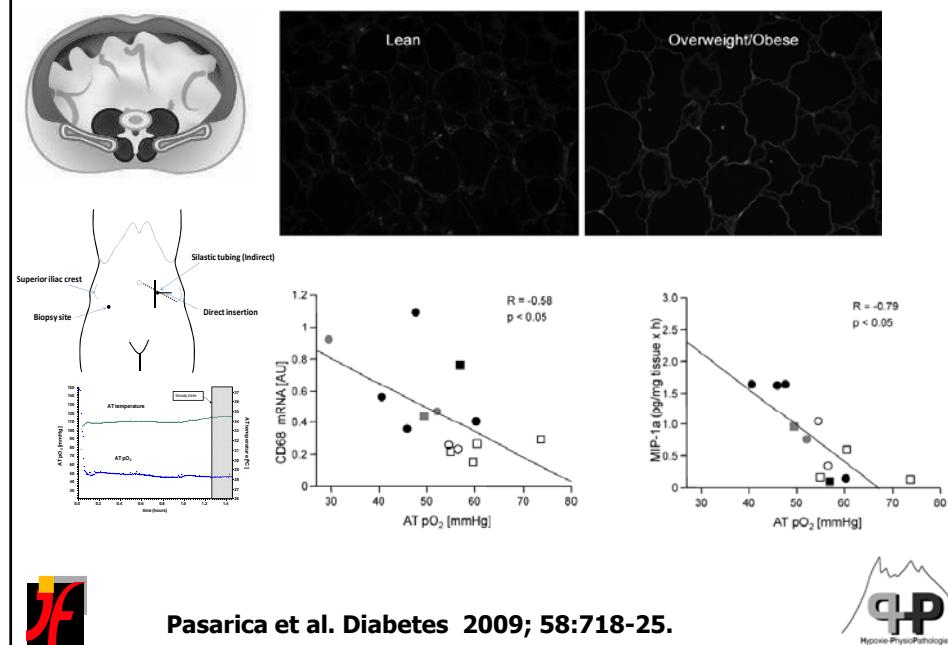
Xu J et al. Free Radical Biology & Medicine 2009;46:783–790

Inserm Hypoxie-Physiopathologie

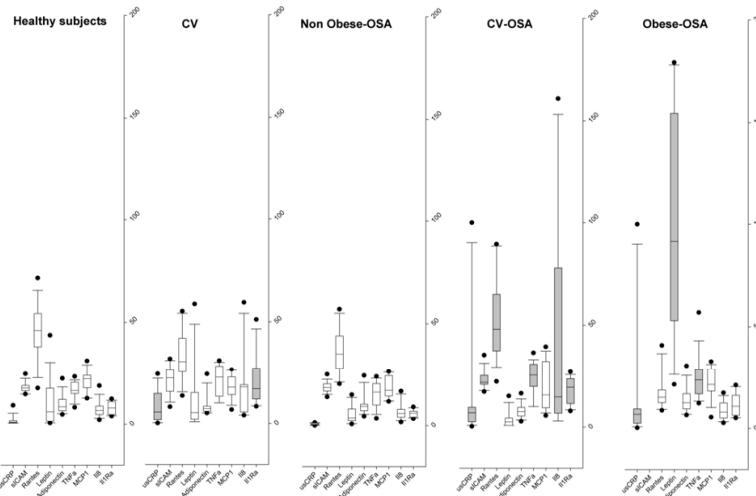
Syndrome d'apnées du sommeil et Diabète



PO₂ locale et inflammation du tissu adipeux



Tissus adipeux, hypoxie et cytokines



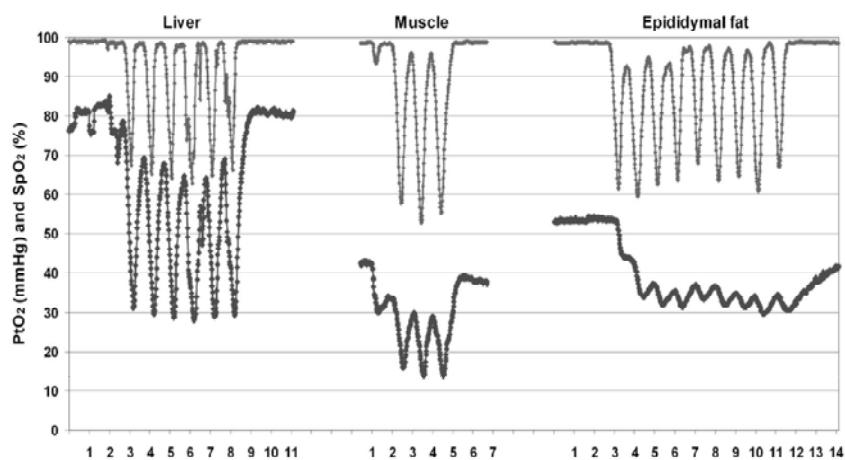
Testelman D et al. Cytokines 2012; Soumis

Inserm

Institut national



La réponse à l'hypoxie intermittente est organe spécifique



Reinke C et al

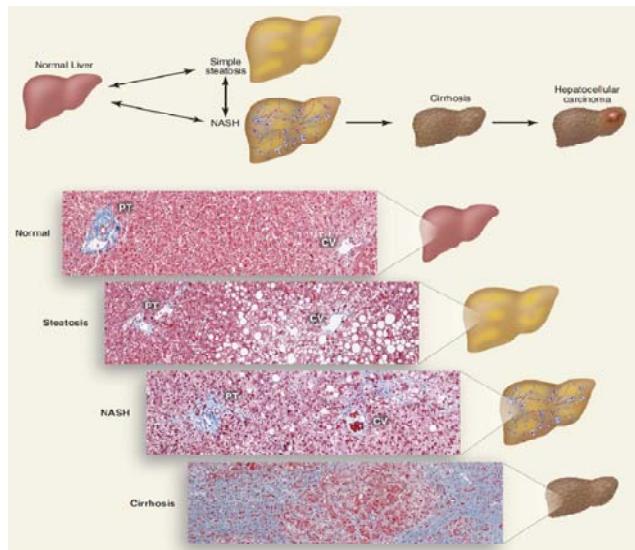
J Appl Physiol 2011

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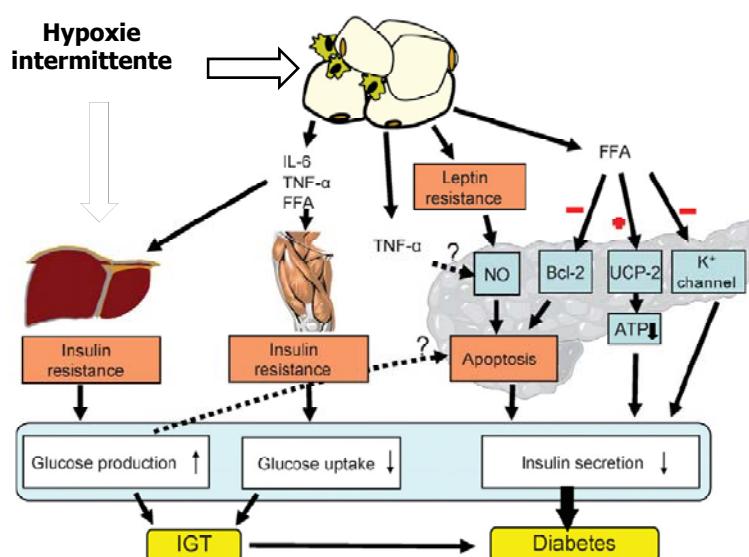
La réponse à l'hypoxie intermittente est organe spécifique



Cohen JC et al. Science 2011;332:1519-23

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Hypoxie-PhysioPathologie



Hajer et al. European Heart Journal 2008;29:2959–2971

Méthodes

- 101 obèses adressés en chirurgie bariatrique
 - Biopsies de foie
 - Biopsies de graisse viscérale et sous-cutanées
- Sévérité des désaturation quantifiée par IDO >3%



Aron-Wisnewsky J et al. J Hepatol 2012, in press



Différentes réponses tissulaires locales à l'hypoxie intermittente

Variable	ODI <6.7 (n = 33)	ODI 6.8-18.5 (n = 34)	ODI >18.5 (n = 34)	p*
Age, years	43.5 ± 9.7	41.4 ± 11.5	48.4 ± 11.3	0.03
BMI, kg/m ²	45.7 ± 5.7	40.6 ± 6.8	48.3 ± 7.0	0.3
Fat mass, kg	58.4 ± 9.8	57.2 ± 12.5	59.2 ± 13.2	0.8
Fat free mass, kg	58.4 ± 9.3	60.0 ± 9.9	62.4 ± 10.9	0.3
ODI, /nour	3.6 ± 2.0	11.7 ± 3.2	34.3 ± 19.8	<0.0001
Mean nocturnal SaO ₂ , %	95.2 ± 1.6	94.7 ± 1.6	93.1 ± 2.8	0.005
Minimal nocturnal SaO ₂ , %	84.9 ± 5.6	80.5 ± 8.4	71.4 ± 12.1	<0.0001
PaO ₂ , mmHg	90.4 ± 9.7	89.6 ± 13.7	91.5 ± 11.3	0.005
Metabolic comorbidities				
Type 2 Diabetes, %	6.1	26.5	38.2	<0.0001
Metformin, %	6.3	1.8	26.5	0.0002
Sulfamides, %	3.0	5.9	17.7	0.004
Glitazone, %	0.0	0.0	2.94	0.1
Dyslipidemia, %	19.4	35.3	54.6	<0.0001
Hypertension, %	12.1	37.5	45.2	<0.0001
Biological parameters				
Fasting glucose, mM	5.6 ± 1.4	5.9 ± 1.9	6.9 ± 3.0	0.04
Fasting insulin, µU/ml	11.7 ± 5.6	18.8 ± 13.3	15.1 ± 9.4	0.02
HOMA index	2.9 ± 1.5	5.7 ± 6.5	4.7 ± 3.3	0.04
Triglycerides, mM	1.3 ± 0.6	1.5 ± 0.9	1.8 ± 1.0	0.1
Leptin, ng/ml	62.9 ± 20.9	64.7 ± 23.0	62.6 ± 28.6	0.9
IL-6, pg/ml	2.7 ± 1.3	3.5 ± 2.2	4.1 ± 2.8	0.03
ALT, IU/L	30.4 ± 19.3	29.7 ± 20.9	33.6 ± 16.3	0.7
AST, IU/L	21.7 ± 7.8	22.9 ± 8.4	23.3 ± 6.6	0.7

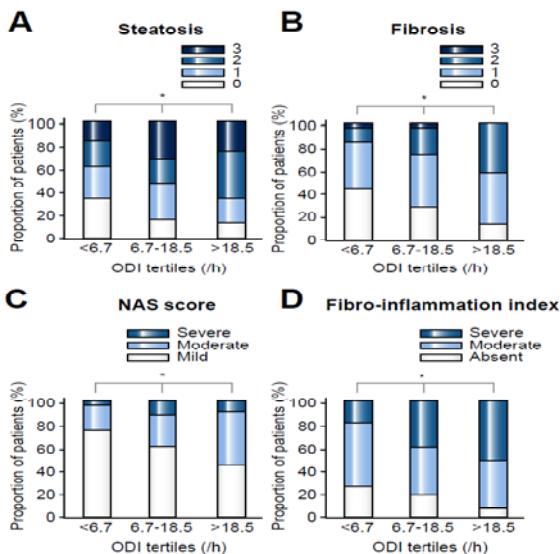
Aron-Wisnewsky J et al. J Hepatol 2012, in press



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Différentes réponses tissulaires locales à l'hypoxie intermittente



Aron-Wisnewsky J et al. J Hepatol 2012, in press

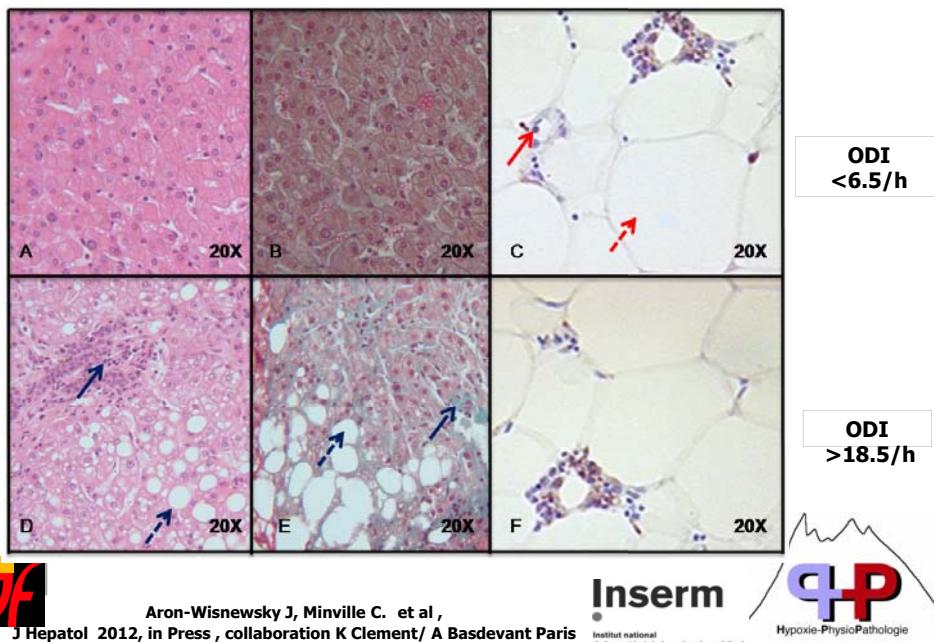


Différentes réponses tissulaires locales à l'hypoxie intermittente

Adipose tissue (AT) histopathology	ODI <6.7	ODI 6.8-18.5	ODI >18.5	p*
Subcutaneous adipocytes size, μm^3	76.8 ± 12.8	77.2 ± 12.5	74.3 ± 11.4	0.6
Omental adipocytes size, μm^3	66.3 ± 13.8	66.9 ± 11.2	68.3 ± 9.3	0.8
Macrophages in subcutaneous AT, n/100 adipocytes	16.4 ± 8.1	17.8 ± 11.0	15.4 ± 8.0	0.6
Macrophages in omental AT, n/100 adipocytes	27.4 ± 12.7	26.6 ± 12.6	30.6 ± 15.1	0.5

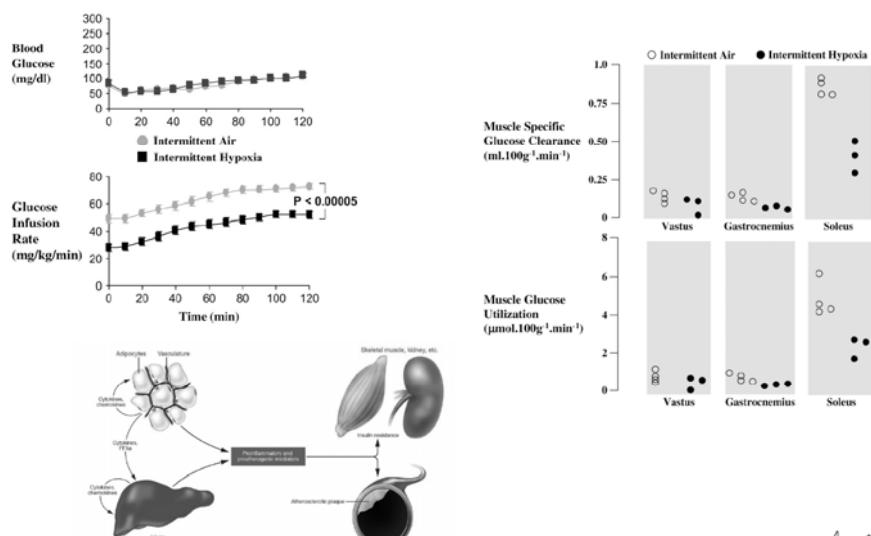


Hypoxie intermittente et foie

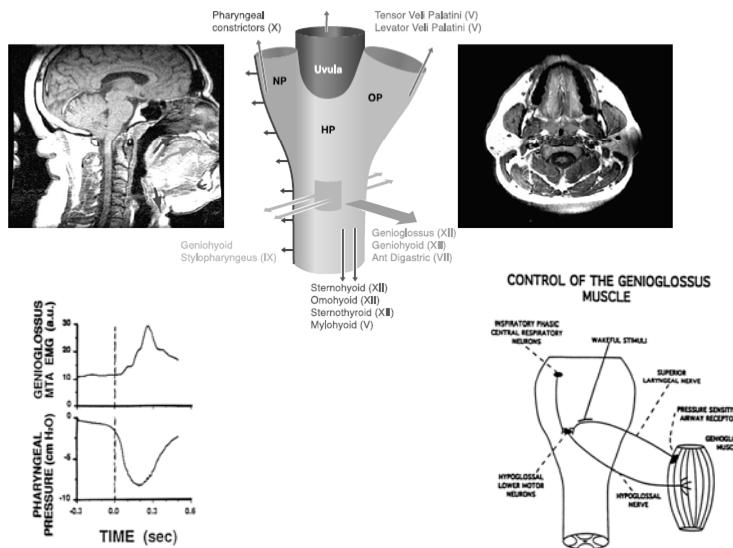


Syndrome d'apnées du sommeil et diabète

Souris en hypoxie intermittente et métabolisme glucidique



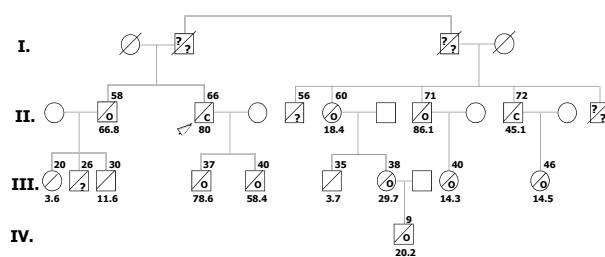
Contrôle de la perméabilité pharyngée : Le reflexe protecteur du pharynx



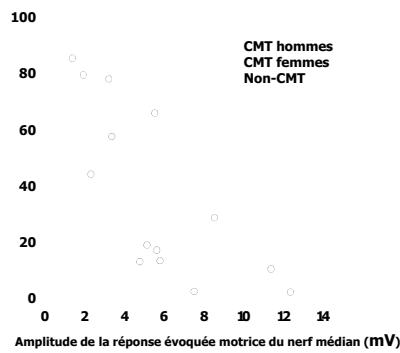
Dempsey et al. Physiol Rev 2010

Neuropathie Héréditaire Charcot Marie Tooth (CMT1A)

Lancet 2001



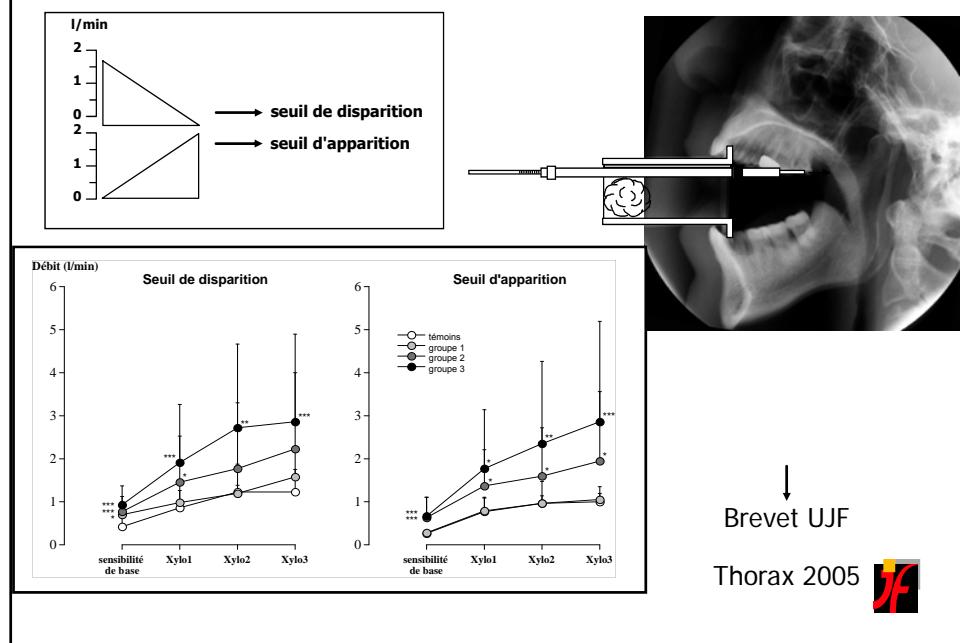
IAH



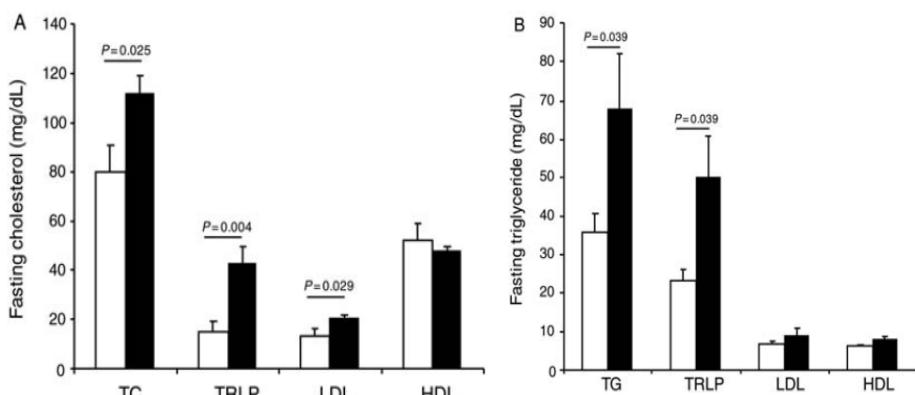
Association systématique CMT1A - SAS
Sévérité du SAS corrélée à la sévérité du CMT



Altération de la sensibilité pharyngée au cours du SAS



Tissus adipeux, dyslipidémie et SAS



Elévation du cholestérol et des triglycérides chez l'animal après 4 semaines d'exposition à l'hypoxie intermittente



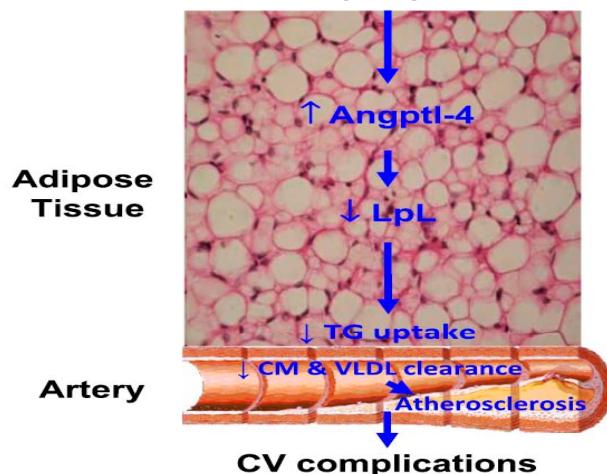
Drager L et al. Eur Heart J 2011, In press

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Hypoxie-PhysioPathologie

Tissus adipeux, dyslipidémie et SAS

Chronic Intermittent Hypoxia (CIH)

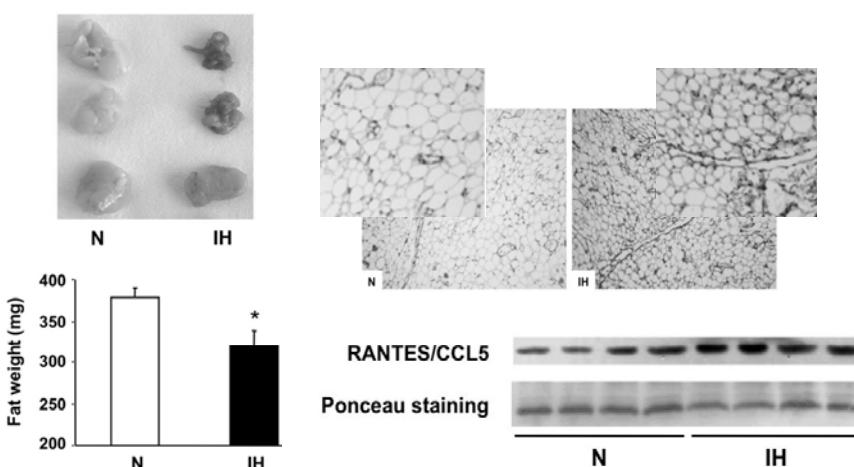


Drager L et al. AJRCCM 2011

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Athérosclérose, IH et tissus adipeux



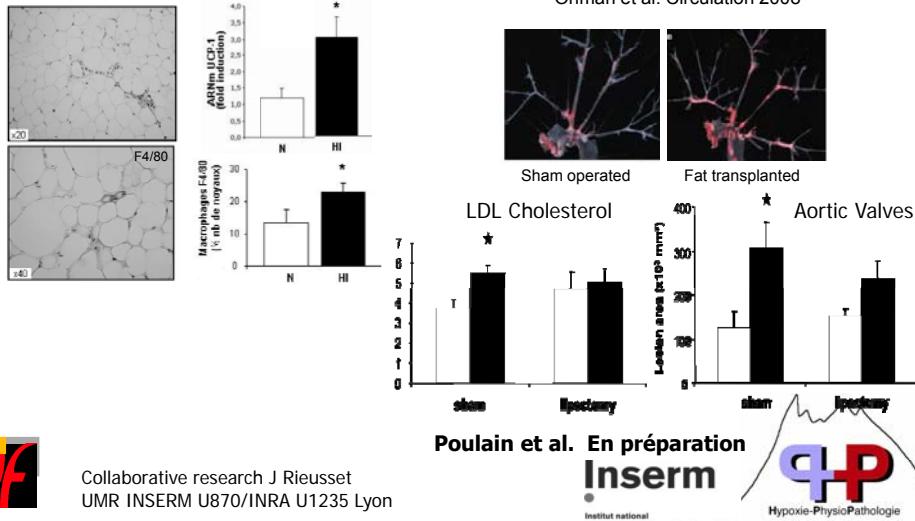
Arnaud et al., En préparation

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Athérosclérose, IH et tissus adipeux

Fat transplantation
Ohman et al. Circulation 2008

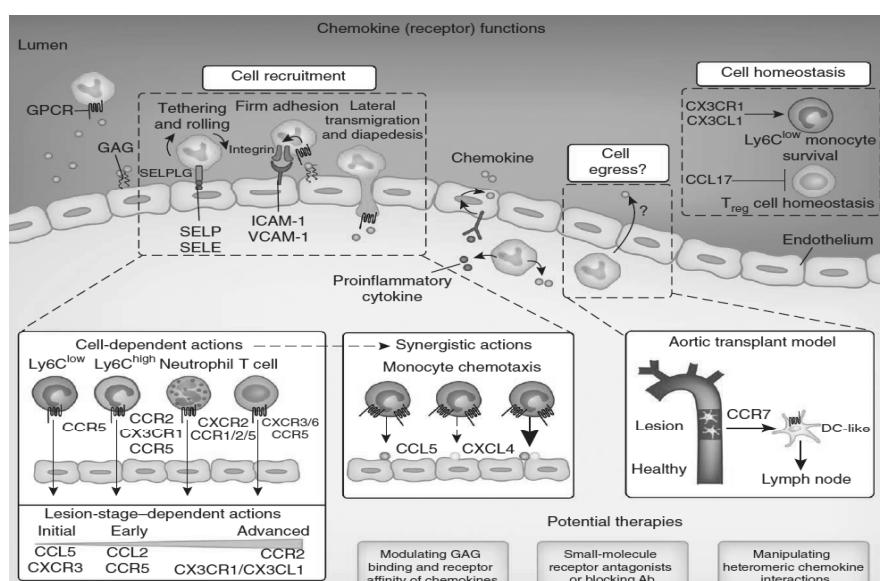


Collaborative research J Rieusset
UMR INSERM U870/INRA U1235 Lyon

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Inflammation et athérosclérose

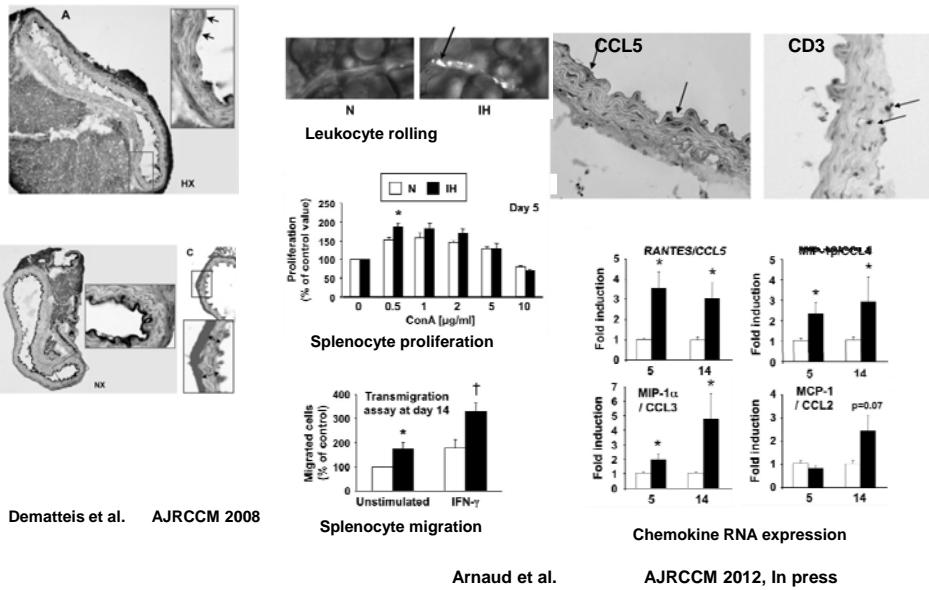


Weber C

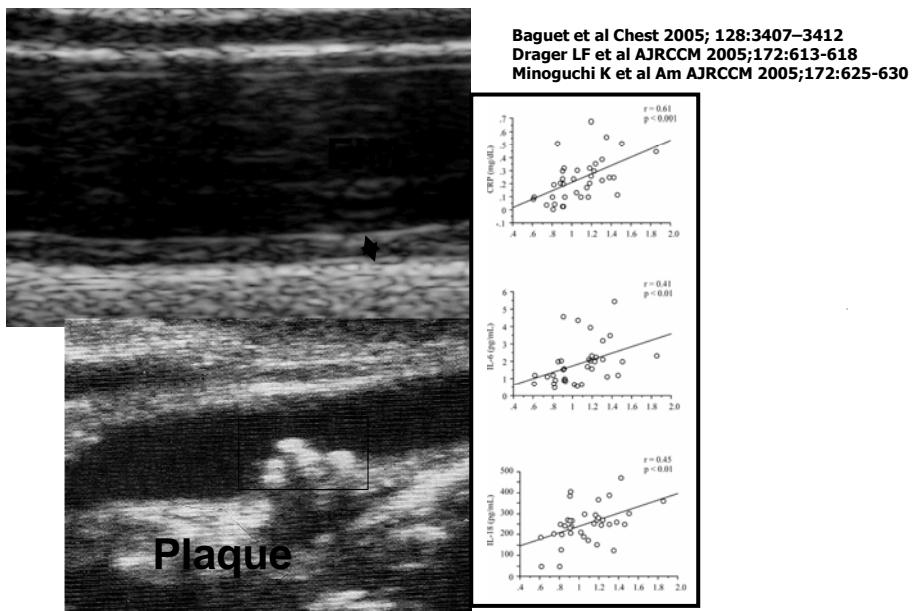
Nature Medicine 2011

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Hypoxie-PhysioPathologie

Remodelage vasculaire et Hypoxie intermittente



Marqueurs CV infra-cliniques

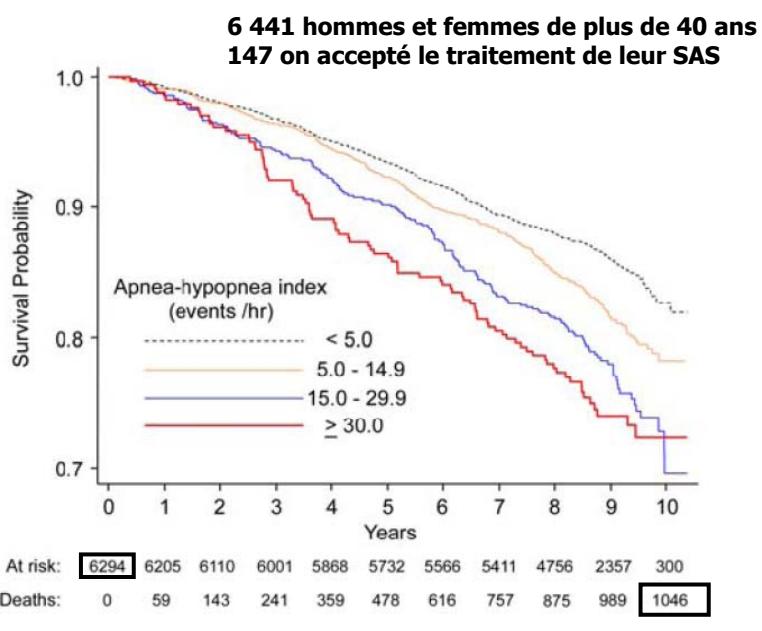


Pathologie coronarienne et SAS

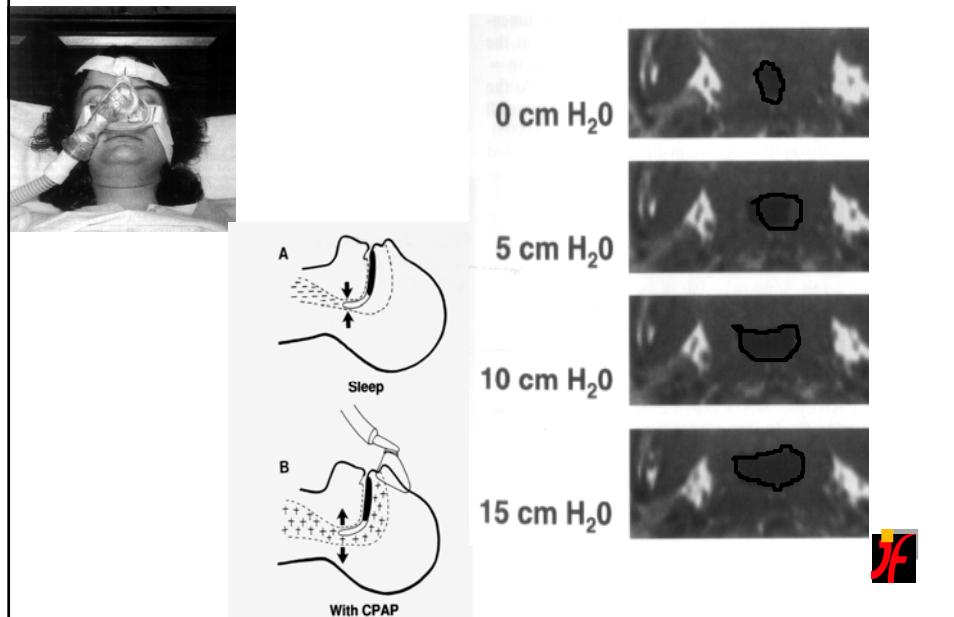
SAOS prédit les accidents coronariens (Infarctus du myocarde, revascularisation coronaire ou décès par accident coronarien) uniquement chez les hommes ≤70 ans

	AHI (Events per Hour)				P†
	<5.0	5.0 to 14.9	15.0 to 29.9	≥30.0	
Men					
Nc. of subjects	829	644	282	172	
Nc. of CHD events	114	95	47	40	
Covariates in model					
Age, race, BMI, smoking	1.00 (Referent)	0.94 (0.71, 1.24)	1.07 (0.75, 1.52)	1.45 (0.99, 2.13)	0.046
Plus total and HDL cholesterol, lipid-lowering medications, diabète mellitus	1.00 (Referent)	0.93 (0.70, 1.23)	1.04 (0.73, 1.48)	1.41 (0.96, 2.07)	0.08
Plus SBP, DBP, use of antihypertensive medications	1.00 (Referent)	0.91 (0.69, 1.20)	1.07 (0.75, 1.52)	1.33 (0.91, 1.95)	0.12
Hommes 40 à 70 ans avec un IAH ≥30 avait 68% de risque supplémentaire pour développer un accident coronarien que ceux ayant un IAH < 5.					
1927 hommes and 2495 femmes ≥40 ans sans pathologie cardiovasculaire à l'inclusion Suivi moyen : 8.7 ans					
Gottlieb DJ et al.	Circulation. 2010;122:352-360				

Cohorte prospective observationnelle : Sleep Heart Health Study

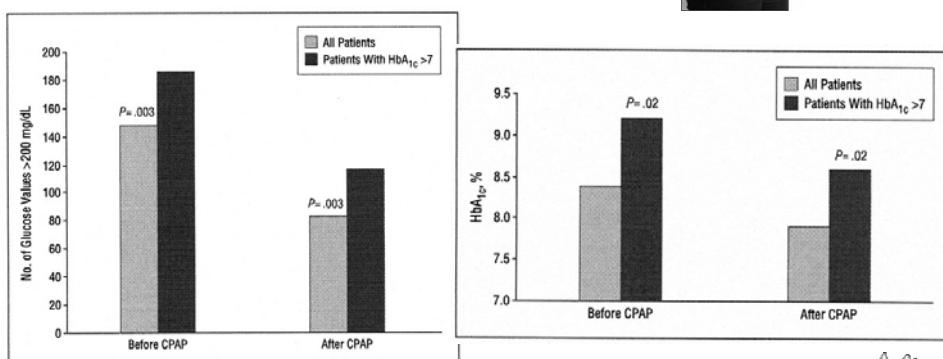
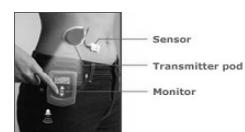


Pression Positive Continue : PPC



Impact de la PPC sur la régulation glycémique

**Capteur sous cutané : 72 heures de monitoring
«continu» de la glycémie (288
mesures/24heures)**
25 diabétiques de type 2



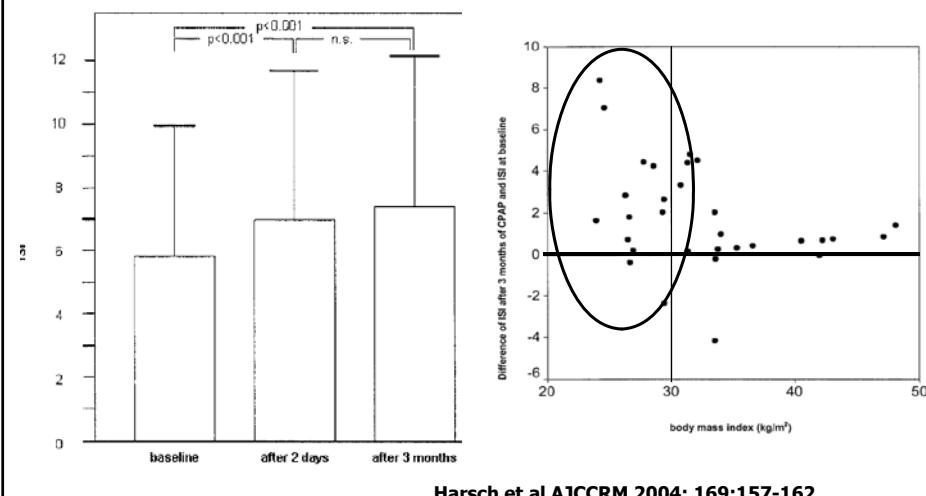
Babu et al. Arch Intern Med 2005

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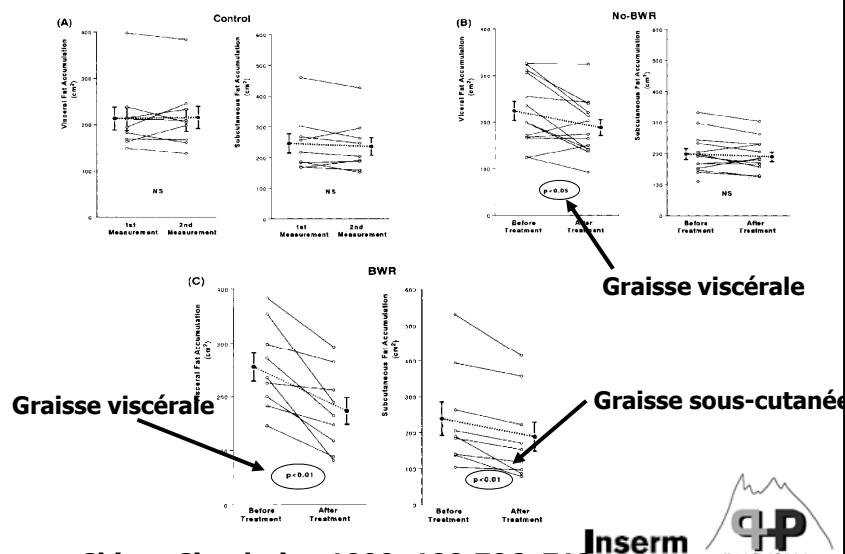
Syndrome d'apnées du sommeil et diabète

TraITEMENT du syndrome d'apnées du sommeil



Effets de la PPC sur la graisse

Graisse viscérale



Chin Circulation 1999; 100:706-712

Effets cumulés du SAS et de l'obésité



Effets métaboliques de la PPC

	Change after therapeutic CPAP	p value	Change after subtherapeutic CPAP	p value	Between group difference	p value (between group changes)
Cholesterol (mmol/l) 3.9-7.8*	-0.28 (0.88) (-0.45 to -0.11) n=104	0.001	-0.07 (0.48) (-0.06 to 0.21) n=107	0.24	0.20 (-0.12 to 0.41)	0.06
Triglyceride (mmol/l) 0.55-1.9* (fasting)	-0.24 (0.26)* (-0.28 to 0.74) n=52	0.37	-0.05 (1.4)* (-0.45 to 0.36) n=49	0.82	0.18 (-0.50 to 0.86)	0.60
FXIIa (ng/ml)†	-0.08 (0.87) (-0.27 to 0.43) n=26	0.65	-0.14 (0.57) (-0.13 to 0.40) n=18	0.30	-0.13 (-0.55 to 0.30)	0.55
FVIIa (mU/ml)†	2.38 (25.1) (-12.5 to 7.8) n=26	0.63	16.3 [26.7] [5.0 to 31.6] n=18	0.01	-20.7 (-36.6 to -4.8)	0.01
s-Psel (ng/ml)†	-4.22 (42.9) (-0.83 to 16.7) n=47	0.50	-7.3 (55.6) (-3.3 to 17.9) n=46	0.17	3.10 (-13.1 to 19.3)	0.71
TAT (ug/l)†	9.31 (43.5) (-26.9 to 8.24) n=26	0.29	1.0 (42.9) (-21.1 to 19.0) n=20	0.91	-8.3 (-34.2 to 17.7)	0.52
vWF Ag (IU/dl) 50-200*	2.1 (22.4) (-8.9 to 4.7) n=44	0.54	-1.8 (24.0) (-5.3 to 8.9) n=46	0.62	3.87 (-5.9 to 13.6)	0.61
Fibrinogen (g/l) 1.5-4.0*	0.05 (0.3) (-0.18 to 0.07) n=26	0.37	-0.03 (0.54) (-0.23 to 0.28) n=20	0.84	-0.08 (-0.33 to 0.18)	0.54
FVII (IU/dl) 50-200*	-5.3 (17.8) (-0.18 to 0.07) n=26	0.14	0.7 (19.1) (-9.2 to 7.7) n=20	0.86	6.0 (-4.7 to 16.8)	0.27
FVIII (IU/dl) 50-200*	-6.0 (19.5) (-1.9 to 13.9) n=26	0.13	0.7 (19.4) (-9.8 to 8.4) n=20	0.87	6.7 (-5.0 to 18.3)	0.26
FXII (IU/dl) 50-200*	-4.1 (16.6) (-2.6 to 10.8) n=26	0.22	8.5 (15.7) (-15.8 to -1.1) n=20	0.03	12.5 [2.8 to 22.2]	0.01
Homocysteine (μmol/l) 5-15*	-0.64 (4.8) (-2.0 to 0.70) n=52	0.34	0.26 (3.4) (-1.23 to 0.72) n=49	0.60	0.18 (-1.51 to 1.87)	0.83



Robinson et al, Thorax 2004

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CHU
Hypoxie-Physiopathologie

Effets métaboliques de la PPC

Eur Respir J 2007; 29: 720-727
DOI: 10.1136/06031936.00043306
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Cardiovascular and metabolic effects of CPAP in obese males with OSA

S.R. Coughlin, L. Mawdsley, J.A. Mugarza, J.P.H. Wilding and P.M.A. Calverley

subjects	intervention	outcome
n= 34 (non diabetic) - AHI 39.7 ± 13.8 - BMI 36.1 ± 7.6	6 weeks CPAP vs. sham CPAP (cross-over!)	- fasting serum glucose, insulin - HOMA - metabolic sy.

Eur Respir J. 29(2007)720



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Effets métaboliques de la PPC

	CPAP	Placebo	Difference (95% CI)	p-value
Subjects n	34	34		
ESS	9.4 ± 0.9	12.5 ± 0.9	-3.1 (-4.5– -1.7)	<0.01
BP mmHg				
Systolic	135.7 ± 2.0	142.4 ± 2.4	-6.7 (-10.1– -3.3)	<0.01
Diastolic	86.8 ± 0.15	91.7 ± 1.6	-4.9 (-8.0– -1.8)	<0.01
Mean arterial	103.1 ± 1.5	108.6 ± 1.7	-5.5 (-8.2– -2.8)	<0.01
BRS $\text{ms} \cdot \text{mmHg}^{-1}$	5.5 ± 0.5	4.5 ± 0.4	1.0 (-0.1– 2.2)	0.07
Fasting glucose $\text{mmol} \cdot \text{L}^{-1}$	4.7 ± 0.1	4.8 ± 0.1	-0.1 (-0.3– 0.03)	0.11
Fasting insulin $\text{pmol} \cdot \text{L}^{-1}$	15.5 ± 1.6	18.1 ± 2.0	-2.6 (-5.9– 0.8)	0.13
HOMA IR	3.3 ± 0.4	3.9 ± 0.5	-0.6 (-1.3– 0.1)	0.08



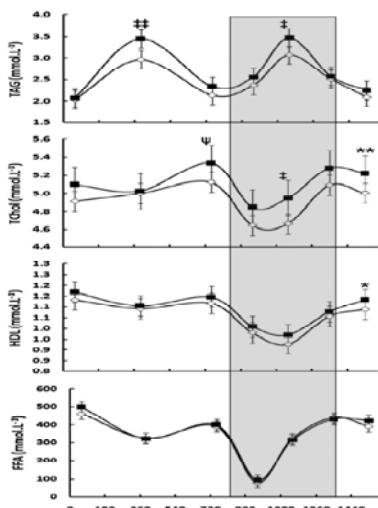
Coughlin SR et al. Cardiovascular and metabolic effects of CPAP in obese males with OSA. Eur Respir J 2007;29:720-727.

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Tissus adipeux, dyslipidémie et SAS

L'hyperlipidémie post prandiale est prédictive des accidents cardiovasculaires



Philips C et al. AJRCCM 2011;184:355-61

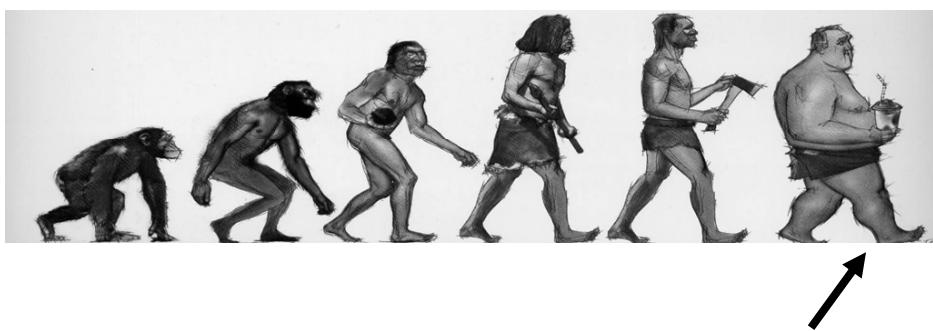
PPC efficace versus inefficace
réduit l'hyperlipidémie post
prandiale

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Institut national de la santé et de la recherche médicale



Syndrome obésité hypoventilation

Définition



- Obésité sévère IMC > 30 kg/m² et PaCO₂diurne > 45 mmHg
- Absence d'autre étiologie connue d'hypoventilation

Olson et al Am J Med 2005

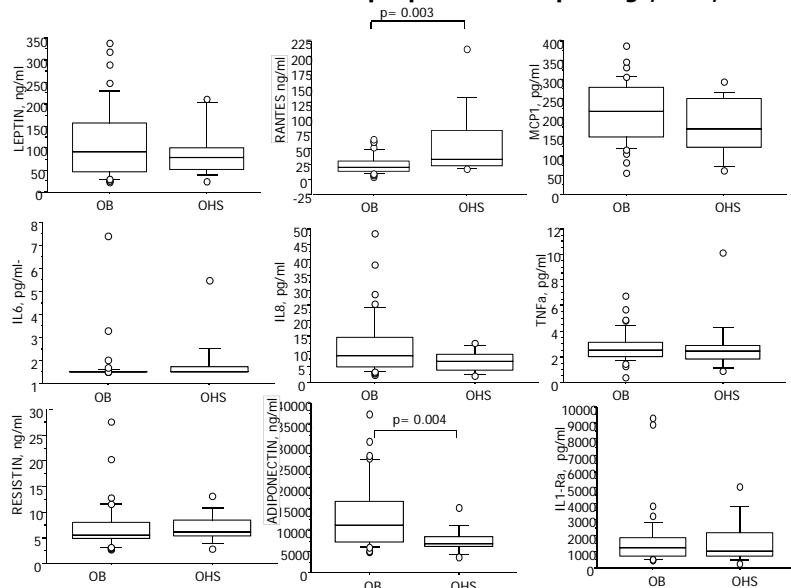


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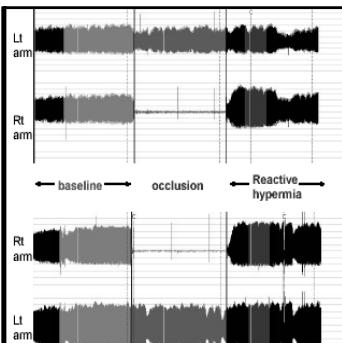
Statut inflammatoire et anti-inflammatoire au cours du SOH

14 SOH versus 39 obèses eucapniques matchés pour age, sexe, IMC



Borel JC

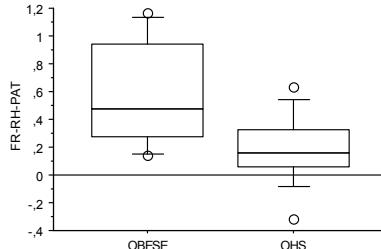
PLoS One 2009;4:e6733.



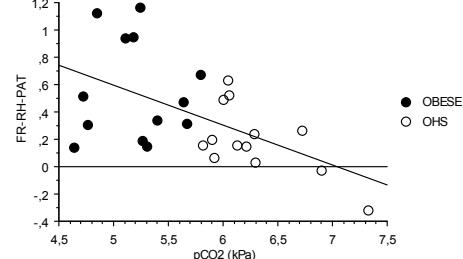
Dysfonction endothélique prédit mortalité cardiovasculaire

Altérée au cours du SOH

En relation avec la PaCO₂ des patients



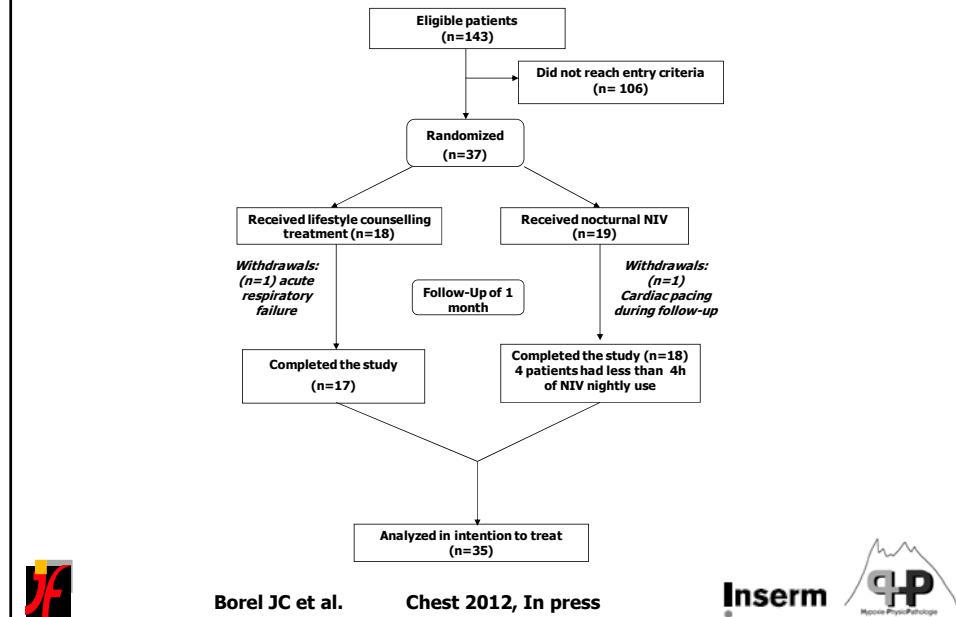
$R=-0.50 \ p=0.013$



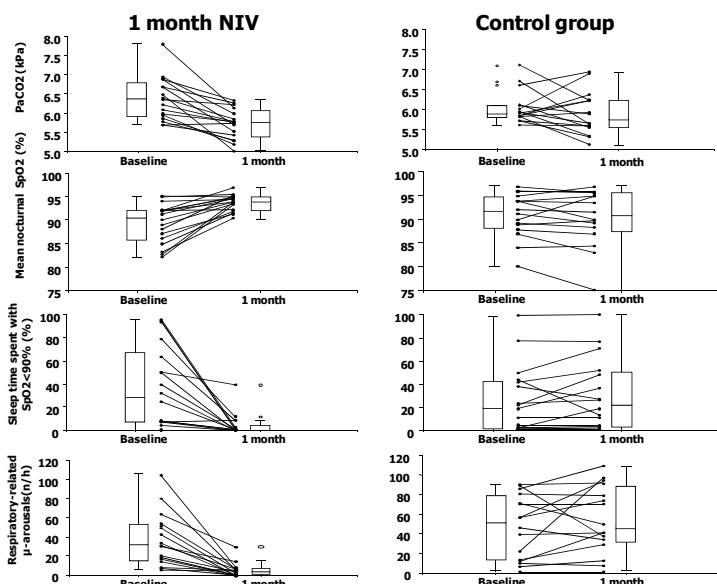
Borel JC

PLoS One 2009;4:e6733.

Essai randomisé contrôlé : VNI versus traitement conservateur



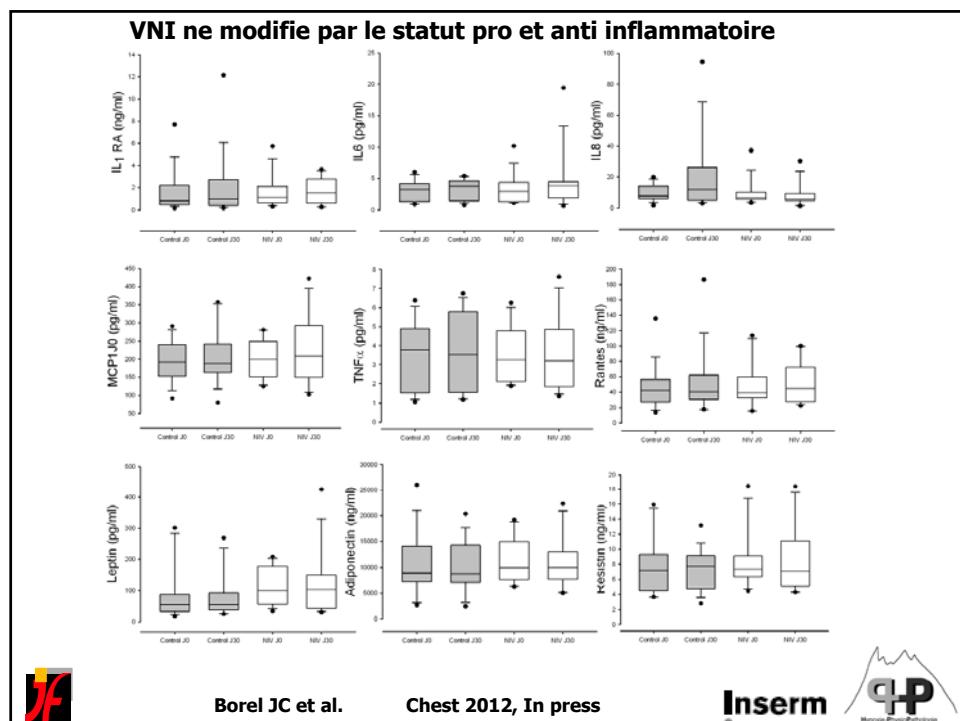
VNI améliore la ventilation diurne et nocturne et la qualité du sommeil



Borel JC et al. **Chest 2012, In press**

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Absence d'impact de la VNI sur les paramètres métaboliques

	Baseline		Effet Traitement				p-value	
	Contrôle		VNI		Contrôle			
	Moyenne ± SD	Moyenne ± SD	Moyenne ± SD	Moyenne ± SD	différence moyenne (95% CI)	différence moyenne (95% CI)		
Glycémie à jeun, <i>mmol.L⁻¹</i>	6,4 ± 2,9	7,6 ± 3,8	0,35 (-0,45; 1,15)	-0,07 (-0,81; 0,67)	ns			
Insuline à jeun, <i>μU.mL⁻¹</i>	12,6 ± 10,9	18,7 ± 17,9	2,96 (-1,19; 7,11)	2,58 (-8,23 ; 13,40)	ns			
HOMA-IR	4,0 ± 4,9	8,6 ± 12,2	1,74 (-0,63 ; 4,10)	2,34 (-6,62 ; 11,30)	ns			
HbA1c, %	6,3 ± 1,1	6,9 ± 2,0	-0,12 (-0,36 ; 0,12)	0,04 (-0,07 ; 0,14)	ns			
Triglycérides, <i>g.L⁻¹</i>	1,46 ± 0,83	1,85 ± 0,57	-0,03 (-0,27 ; 0,20)	0,31 (-0,03 ; 0,65)	ns			
Cholestérol Total, <i>g.L⁻¹</i>	1,89 ± 0,51	2,01 ± 0,44	-0,15 (-0,30 ; -0,01)	-0,17 (-0,33 ; -0,01)	ns			
LDL, <i>g.L⁻¹</i>	1,18 ± 0,45	1,17 ± 0,36	-0,14 (-0,29 ; 0,01)	-0,21 (-0,37 ; -0,05)	ns			
HDL, <i>g.L⁻¹</i>	0,46 ± 0,15	0,43 ± 0,12	-0,01 (-0,05 ; 0,02)	0,01 (-0,03 ; 0,03)	ns			
CHOL/HDL	4,43 ± 1,37	4,73 ± 1,07	-0,20 (-0,69 ; 0,28)	-0,37 (-0,72 ; -0,01)	ns			

Borel JC et al. Chest 2012, In press

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Logo: HypoPP

Promouvoir l'activité physique ne réduisant l'essoufflement à l'effort

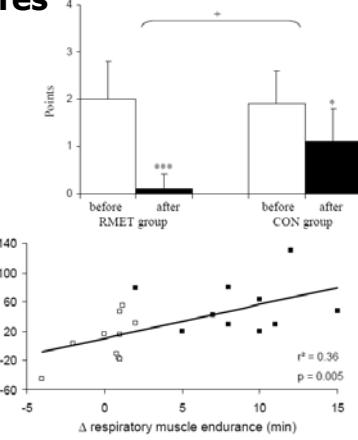
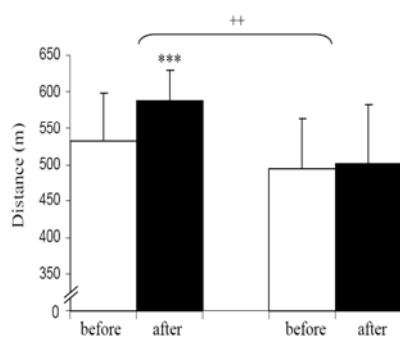


VNI à l'effort



Entraîner les muscles respiratoires

Entraîner les muscles respiratoires

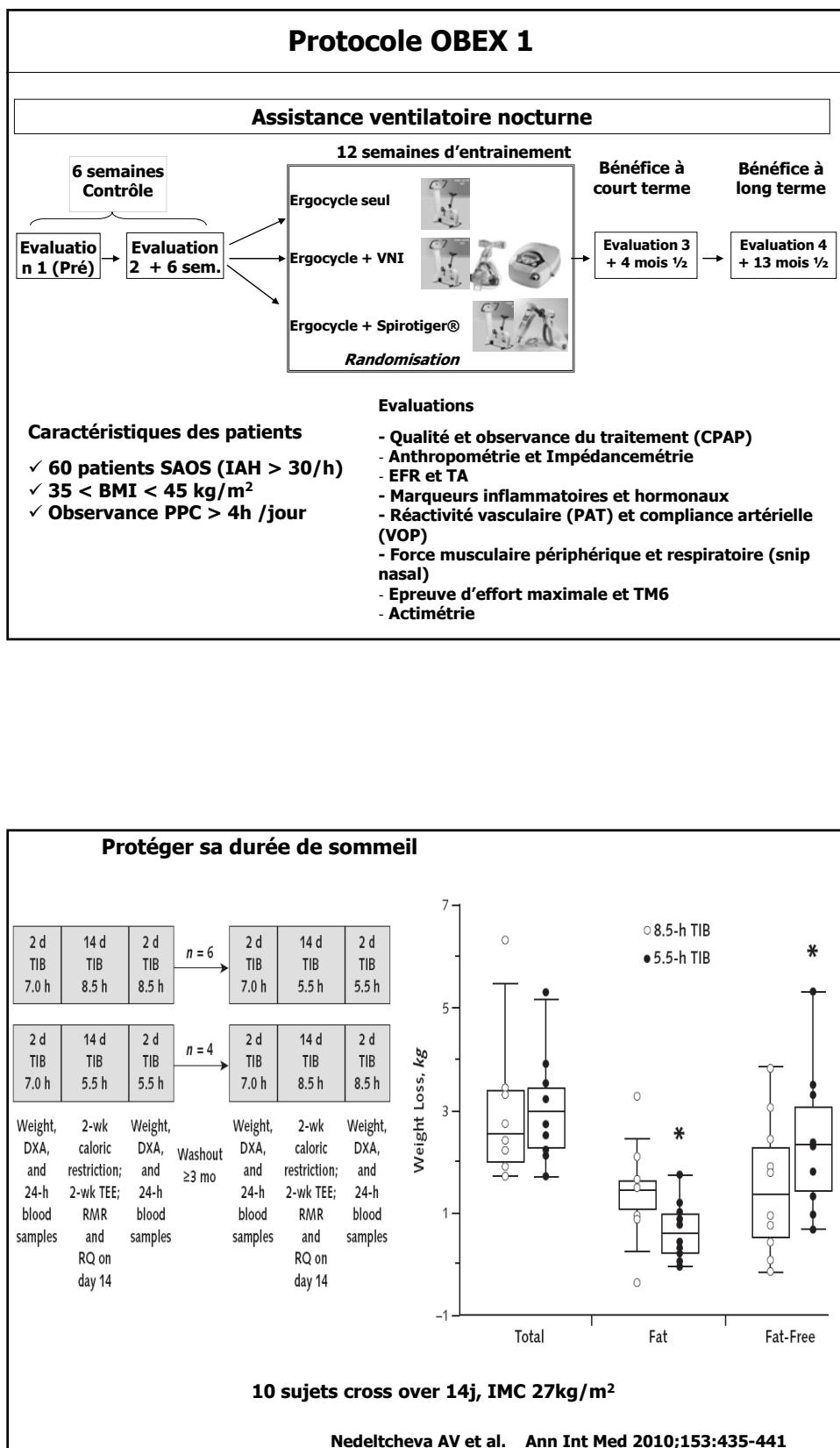


Spirotiger®

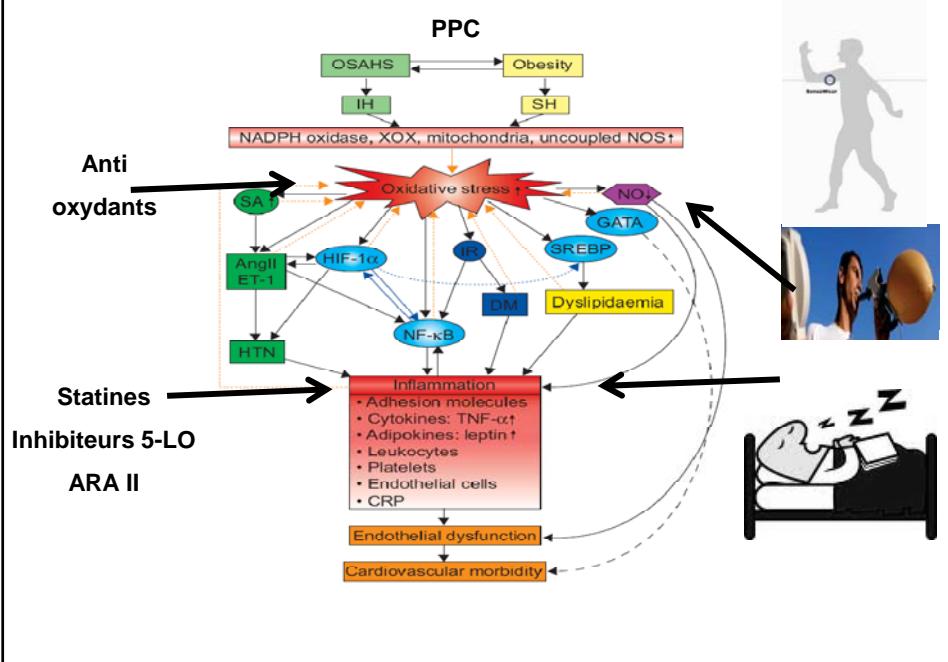


30-min isocapnic hyperpnoea at 60-80% MVV, 3-4 times per week

Villiot-Danger JC et al. Int J Obesity 2010;

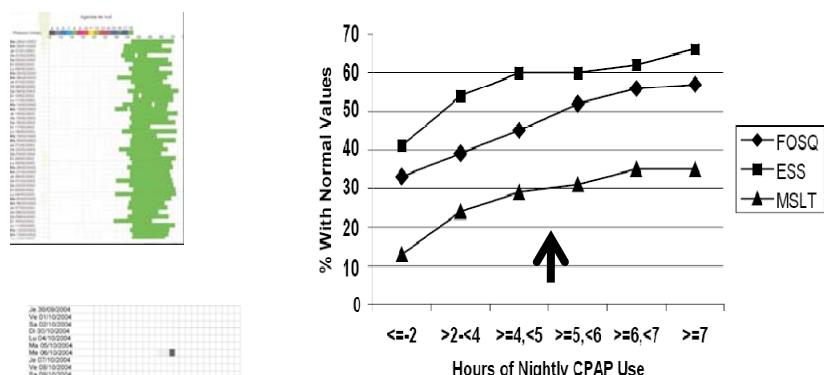


Offrir des modalités thérapeutiques complémentaires



Relation dose-réponse entre observance et amélioration de la somnolence et de la qualité de vie

Observance de la PPC



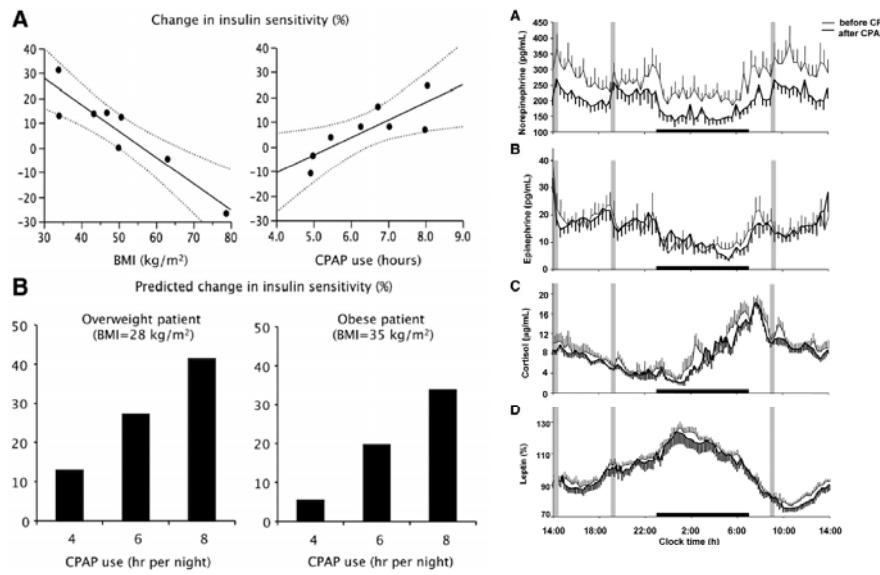
Weaver T et al. SLEEP 2007;30:711-719

N=149

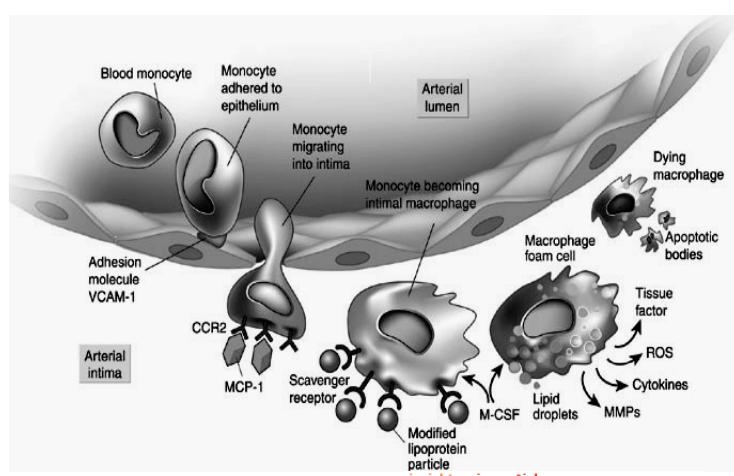
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Impact de la PPC sur la régulation glycémique



Inflammation et athérosclérose



Inflammation in atherosclerosis

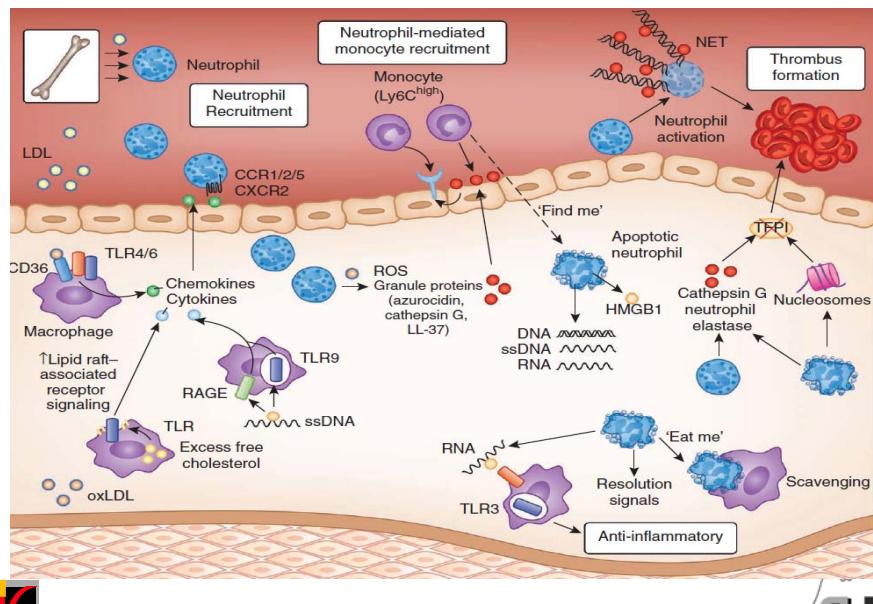
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NATURE | VOL 420 | 19/26 DECEMBER 2002 |

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Inflammation et athérosclérose



Weber C

Nature Medicine 2011

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