SLEEP-DISORDERED BREATHING IN CHILDREN - OVERVIEW

יעקב סיון

מכון ריאות, טיפול נמרץ והמרכז לרפואת שינה

בי"ח "דנה" לילדים, המרכז הרפואי תל-אביב

"I have often imagined the monster of sleep as a heavy, giant head with a tapering body held up by the crutches of reality. When the crutches break we have the sensation of falling."

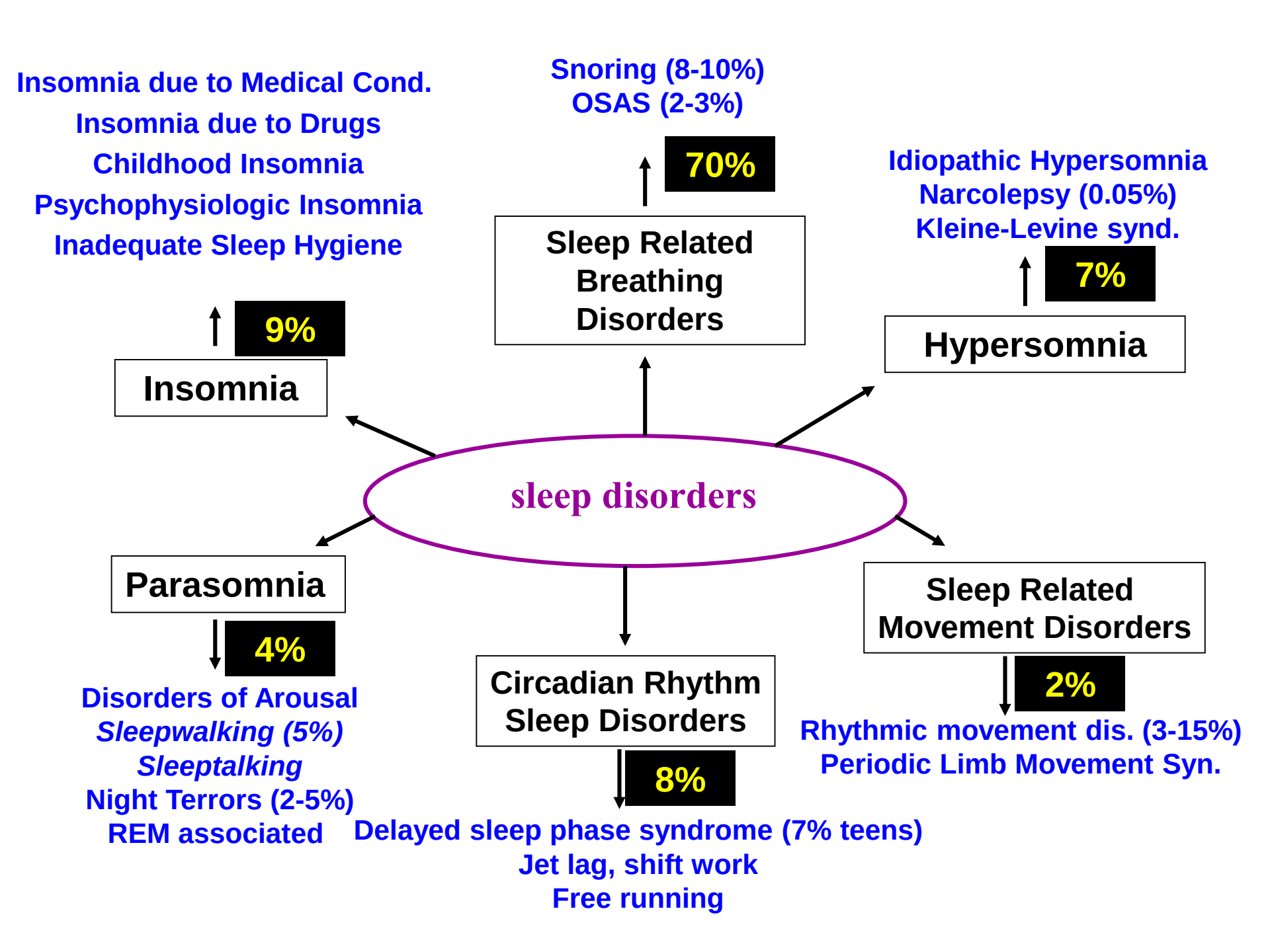
Salvador Dali, 1937

חיפ"פ מצפה הימים גלי כנרת 27.3.2015

Talk outline

- SDB types
- pathogenesis and pathophysiology
- epidemiology & risk factors
- systemic involvement (inflammation, metabolic, CVS, brain)
- morbidity & sequalae (long & short term)
- co-morbidities (obesity, asthma)
- diagnosis (techniques)
- treatment and outcome results

  (surgical, mechanical, medical)

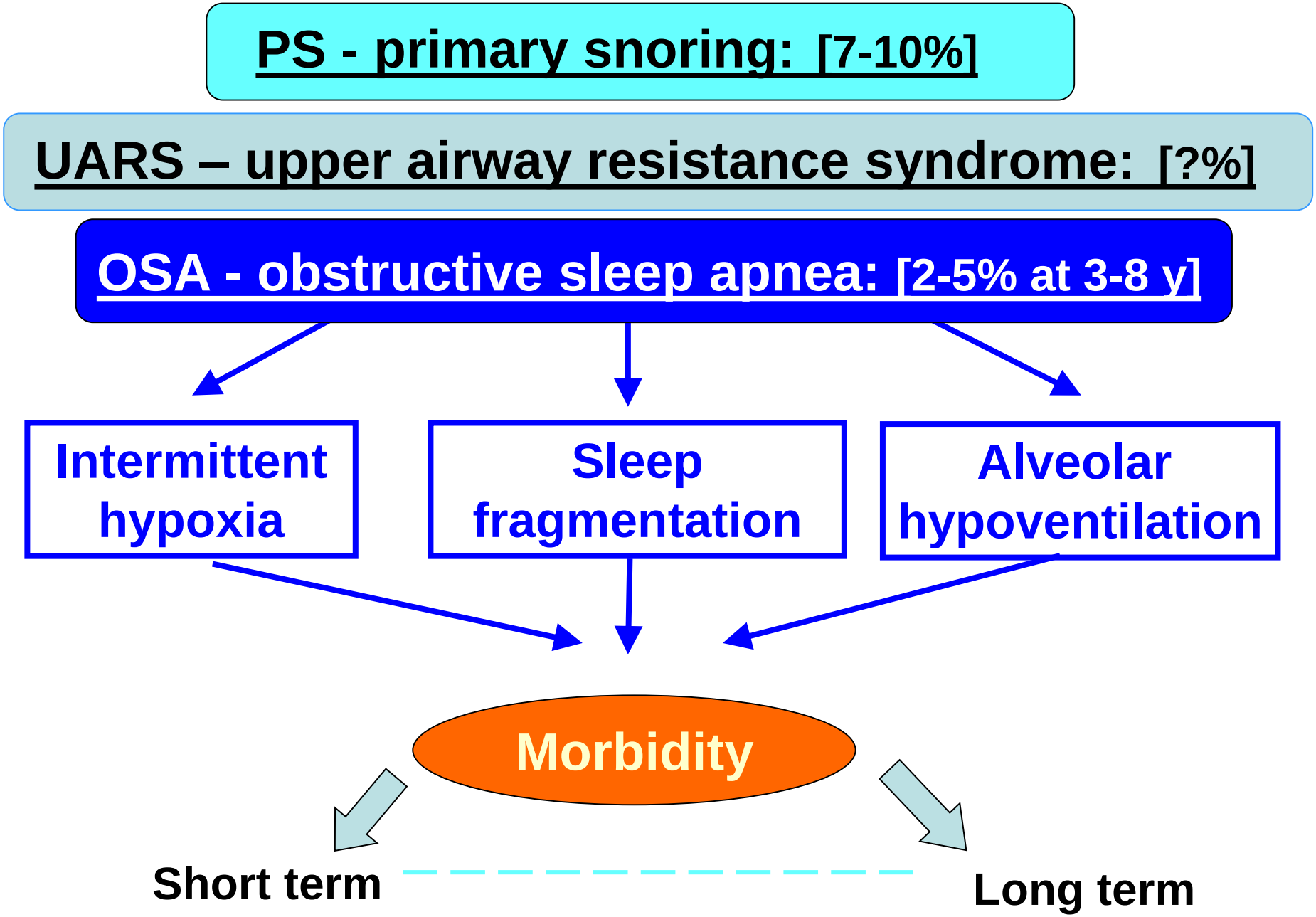

Insomnia due to Medical Cond.
Insomnia due to Drugs
Childhood Insomnia
Psychophysiologic Insomnia
Inadequate Sleep Hygiene
9%
Insomnia
Snoring (8-10%)
OSAS (2-3%)
70%
Sleep Related Breathing Disorders
Idiopathic Hypersomnia
Narcolepsy (0.05%)
Kleine-Levine synd.
7%
Hypersomnia
sleep disorders
Parasomnia
4%
Disorders of Arousal
Sleepwalking (5%)
Sleeptalking
Night Terrors (2-5%)
REM associated
Circadian Rhythm Sleep Disorders
8%
Delayed sleep phase syndrome (7% teens)
Jet lag, shift work
Free running
Sleep Related Movement Disorders
2%
Rhythmic movement dis. (3-15%)
Periodic Limb Movement Syn.

14 SLEEP Journals - 2015

- Sleep
- Sleep Medicine
- Sleep Medicine Reviews
- Sleep and Biological Rhythms
- Behavioral Sleep Medicine
- Journal of Sleep Research
- Sleep and Breathing
- Sleep Research
- Sleeping and Waking
- Open sleep Journal
- Sleep Medicine Clinics of North America
- Journal of Clinical Sleep Medicine
- Sleep Medicine Clinics of North America
- Sleep and Hypnosis

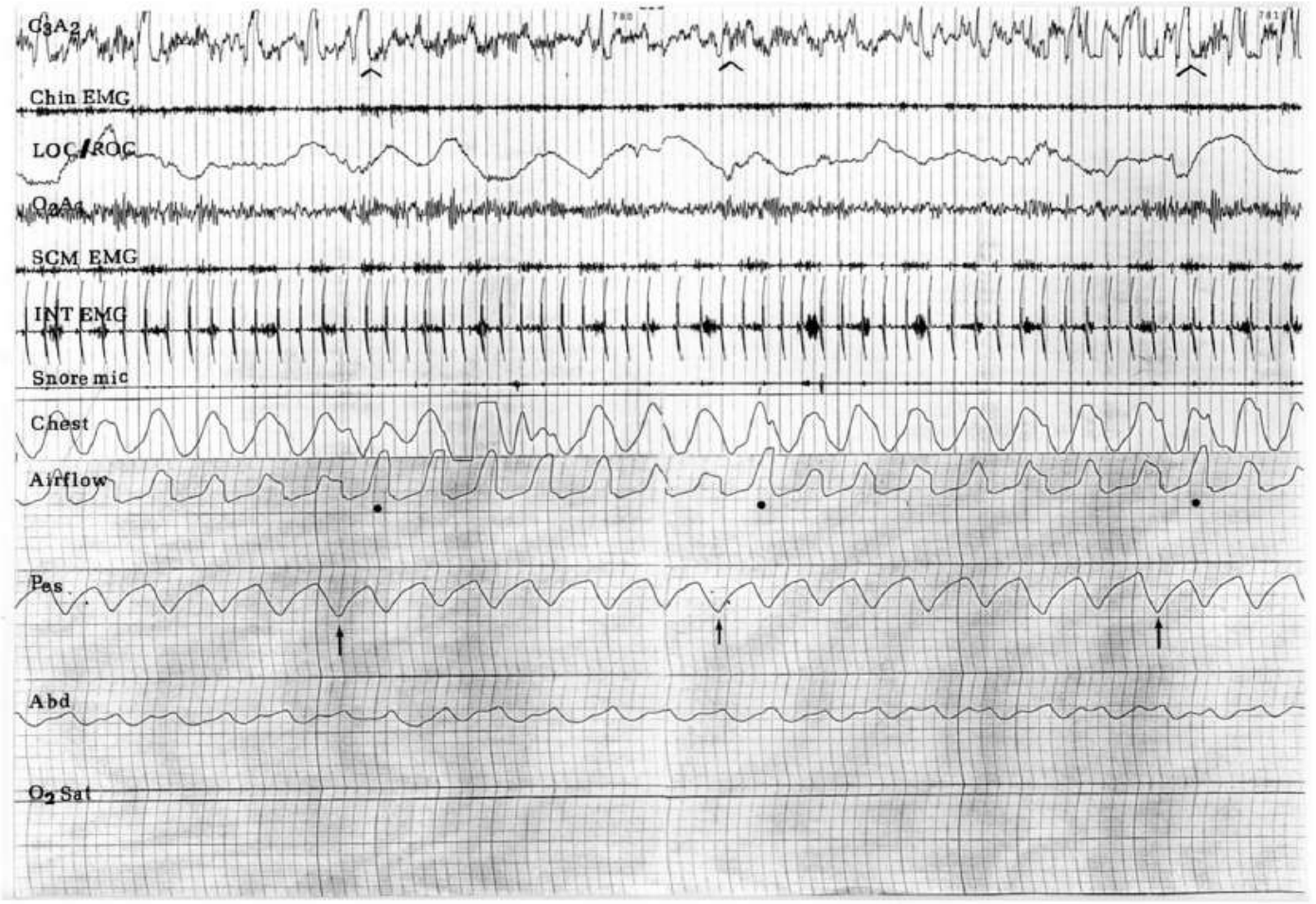
SDB in children recent 5 y. (En) = 1,352 papers - 22/m

SDB & OSAS


PS - primary snoring: [7-10%]
UARS – upper airway resistance syndrome: [?%]
OSA - obstructive sleep apnea: [2-5% at 3-8 y]
Intermittent hypoxia
Sleep fragmentation
Alveolar hypoventilation
Morbidity
Short term
Long term

UARS – upper airway resistance syndrome

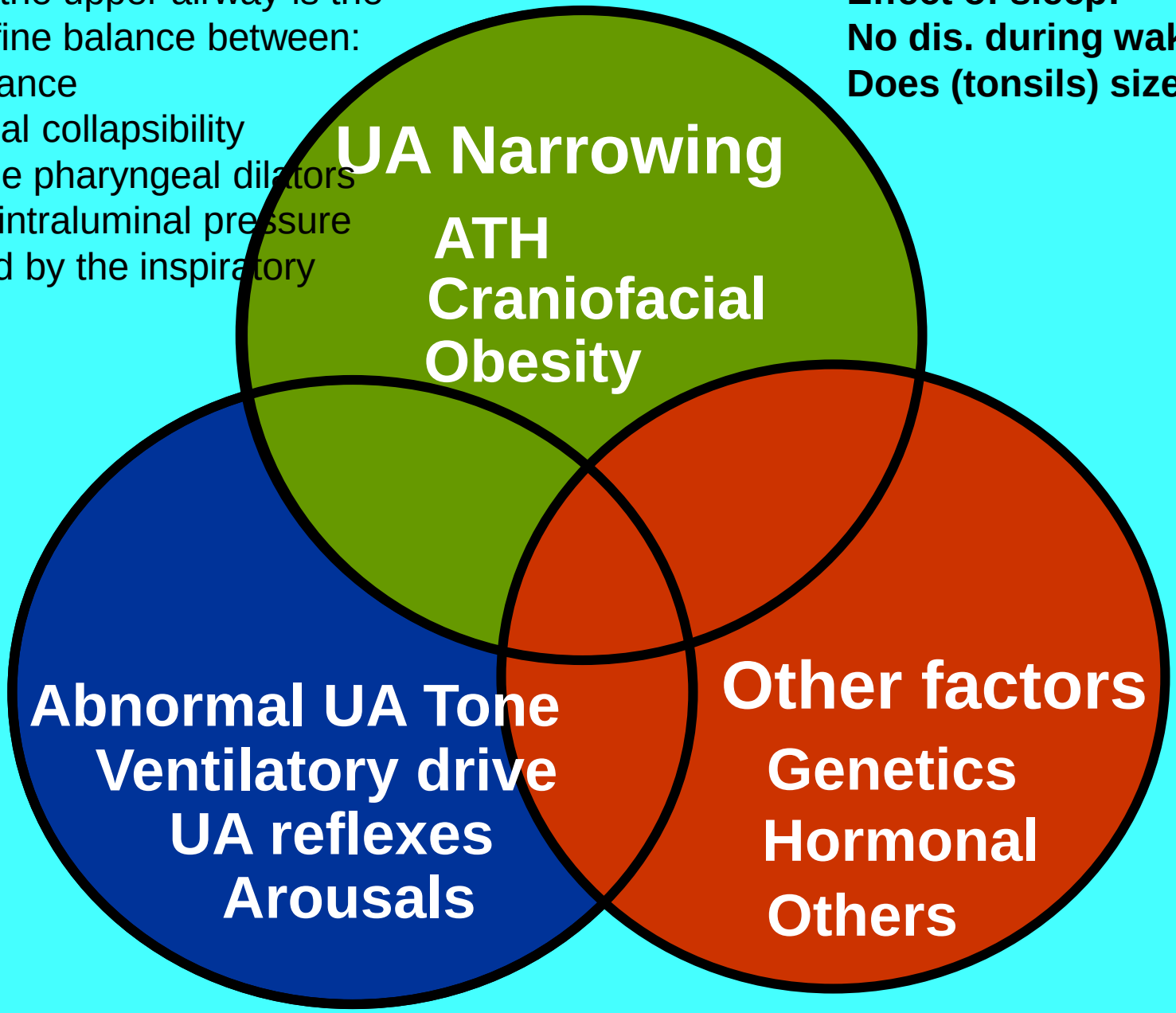
snoring, progressive increased neg. intrathoracic pressure to flow limitation, arousals (RERAs), sleep disruption (abnormal physiology) **without** gas exchange abnormalities (no A/H). Associated with neurobehavioral changes similar to OSAS. Responds to similar treatments.



patency of the upper airway is the result of a fine balance between:

- UA resistance
- pharyngeal collapsibility
- tone of the pharyngeal dilators
- negative intraluminal pressure generated by the inspiratory muscles.

Effect of sleep:
No dis. during wake
Does (tonsils) size matter?



Sleep hypotonia, ATH, obesity

↓

Airway collapse and hypopneic
or apneic events / hypercarbia / hypoxemia

↓

UA resistance increases

↓

UA negative pressure increases

↓

UA pressure receptors are activated

↓

Reflex activation of the UA muscles and increasing
their tone, excessive respiratory effort

↓

EEG arousals

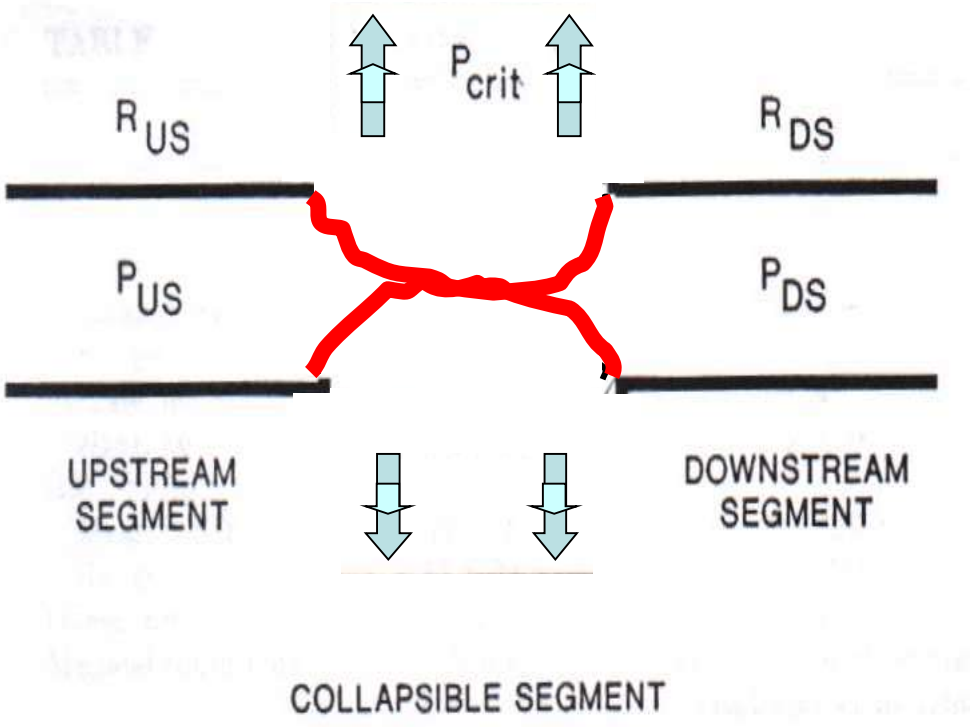
↓

Further increased sympathetic tone, reactivation of the pharyngeal
dilator muscles restoration of the pharyngeal airway patency

↓

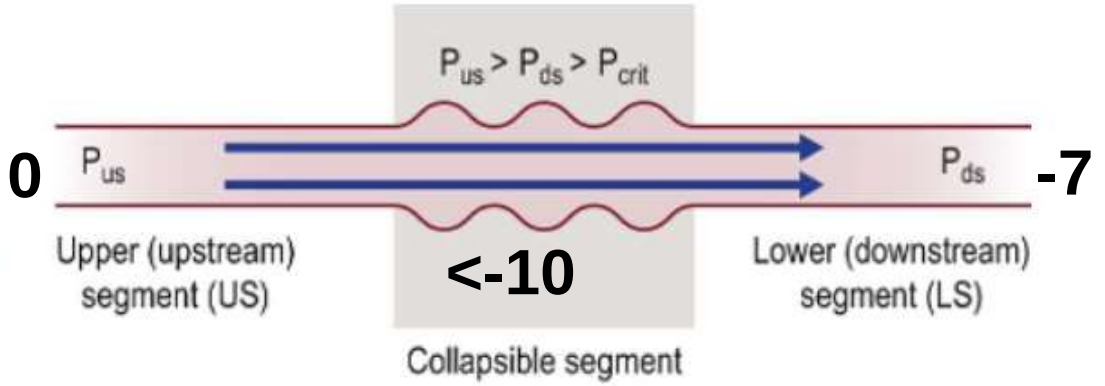
Airflow is possible

ASSESSMENT OF THE UPPER AIRWAY MECHANICAL PROPERTIES

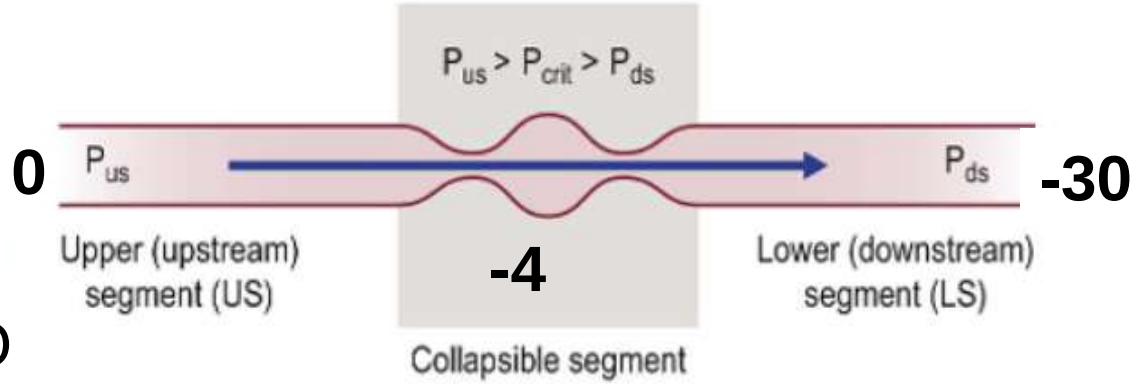


Flow limitation $\Delta P = F \times R$

Normal unobstructed breathing
Open upper airways

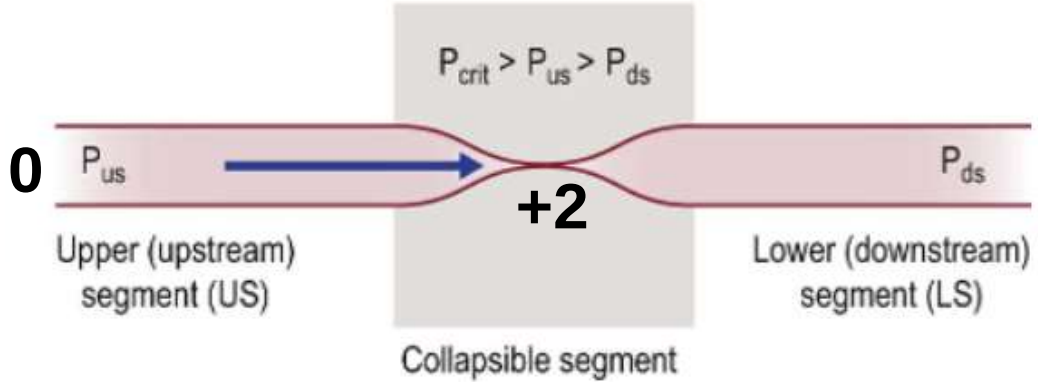


Snoring, UARS, hypopnea
Upper airway collapse with reduced airflow



sleep hypotonia +UAO

Obstructive apnea
Complete occlusion of the upper airway, no airflow



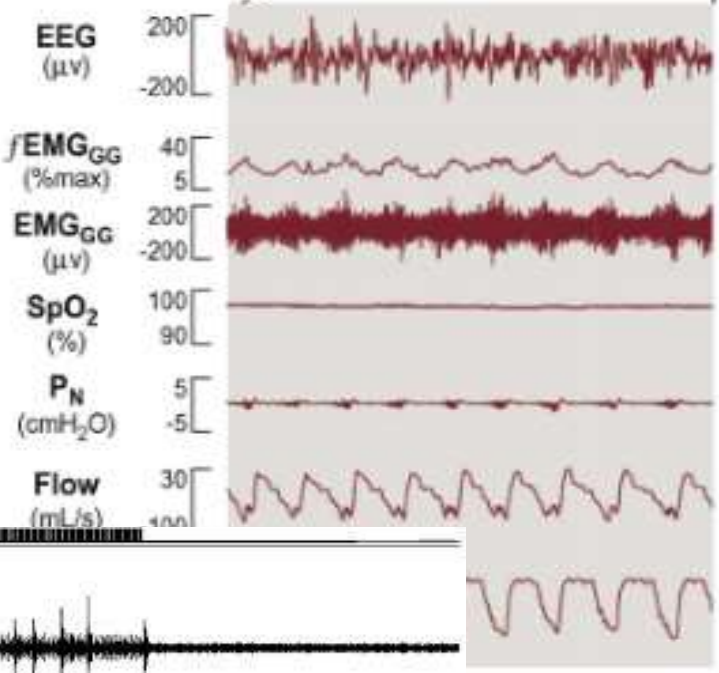
Measurement of the pressure-flow relationships is an objective laboratory tool for the evaluation of the UA function.

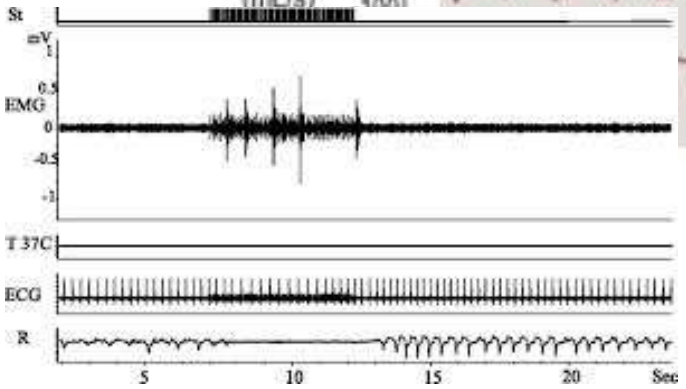
Holding pressure

Active state ↓P_N

P_N Holding P_N

measure of airway collapsibility

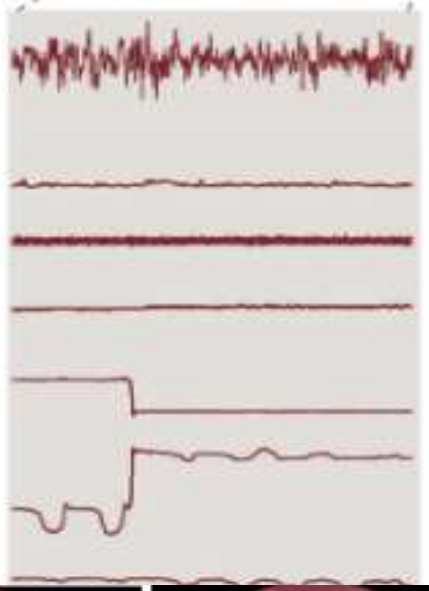


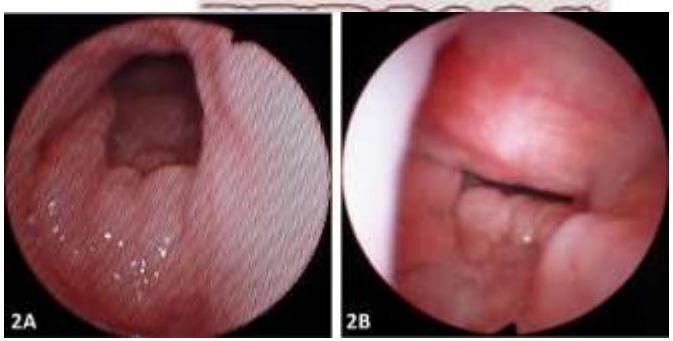


Passive state ↓P_N

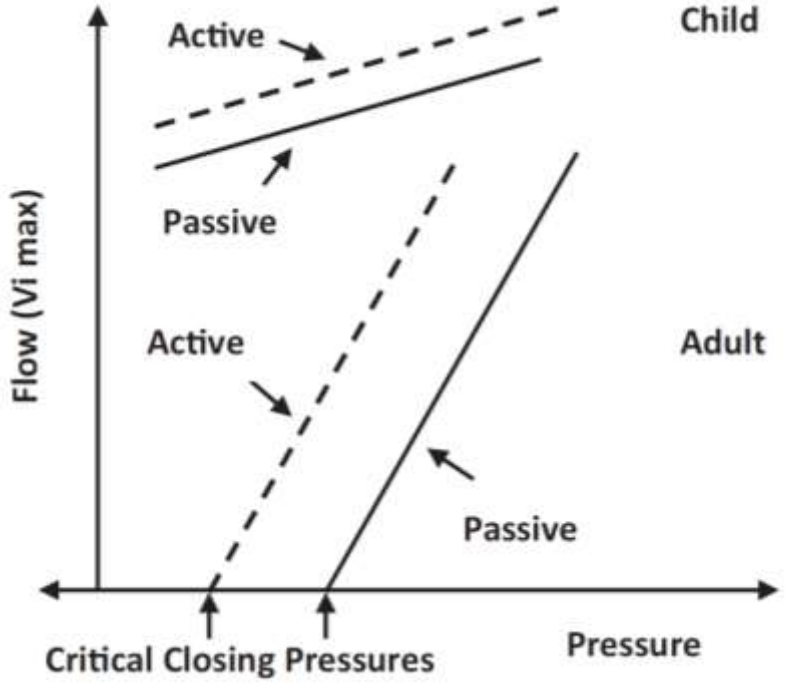
Holding pressure

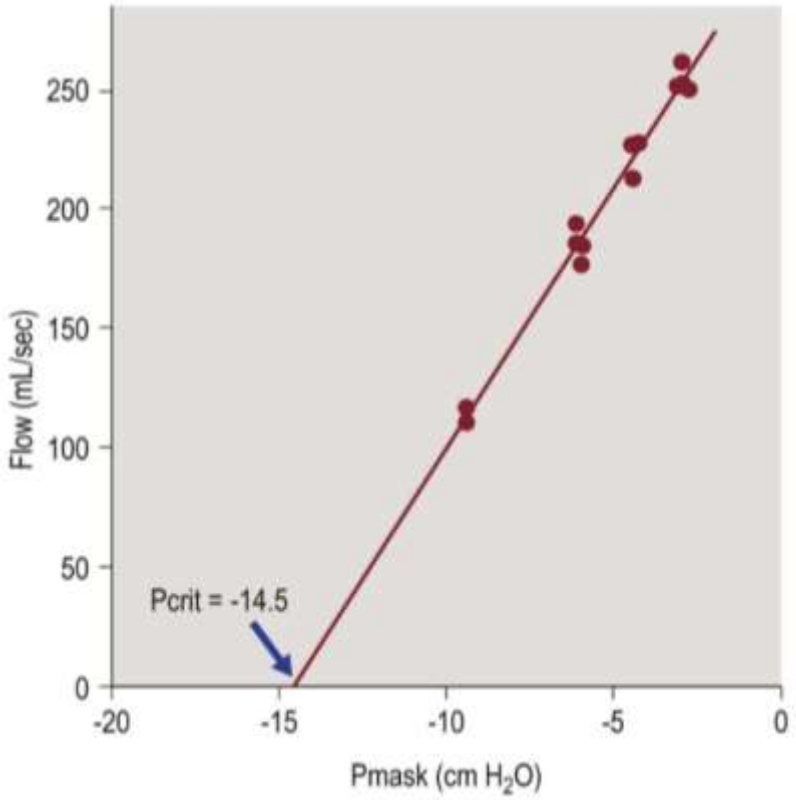
estimates mechanical and structural properties of the airway (w. compensation)





The pediatric airway is very resistant to collapse compared to the adult airway; airway collapsibility increases with age during adolescence and is not a function of pubertal development.



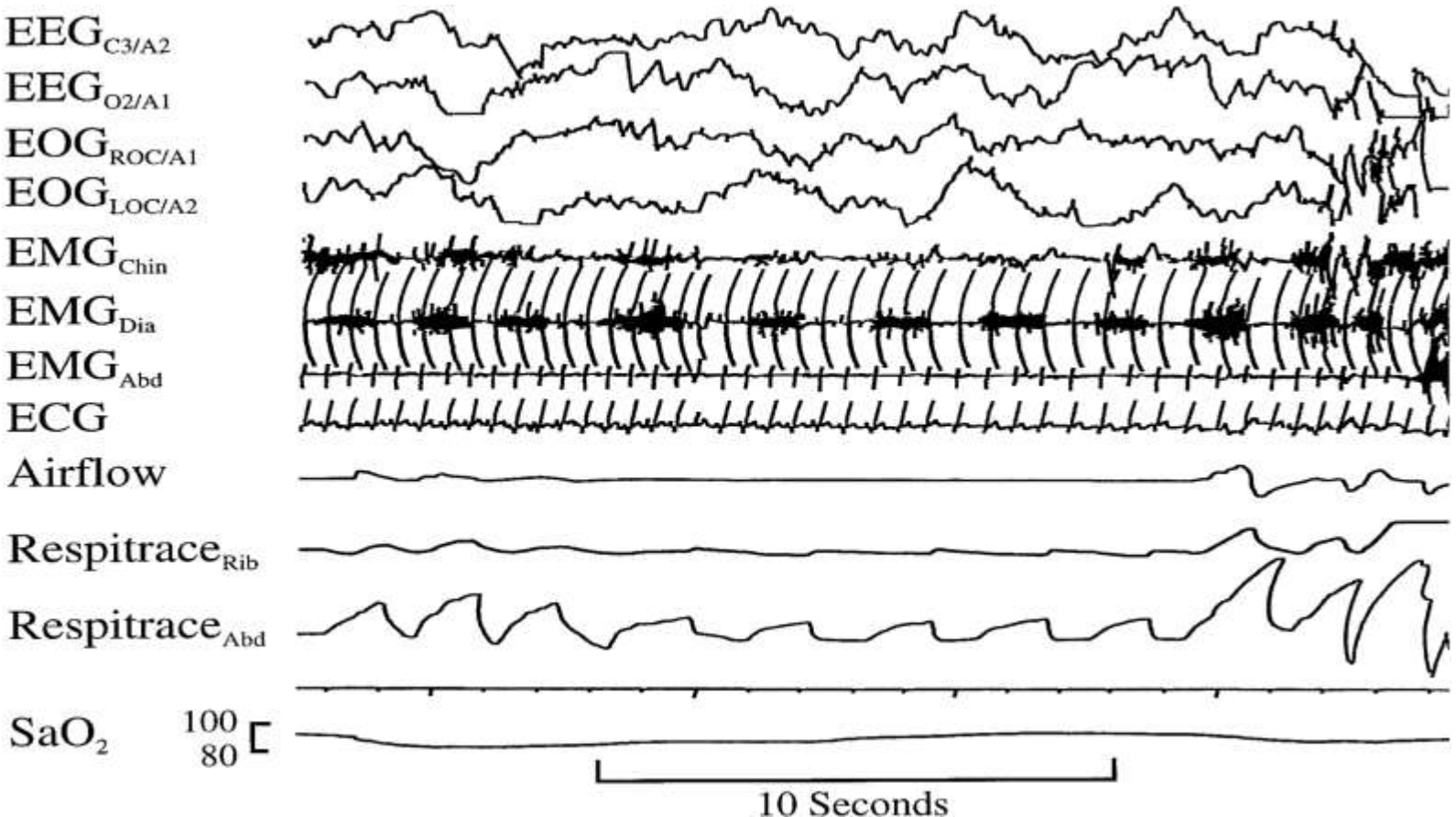


In children and adolescents with OSAS the critical closing pressure is much higher than in non-OSAS children (1±3 cm H2O)

Arousals

A normal phenomenon ≤ 11/h. (respiratory vs. non-respiratory).

Arousals protect from OSAS (increased dilator muscle activity, reduced upper airway resistance, restoration of normal ventilation).



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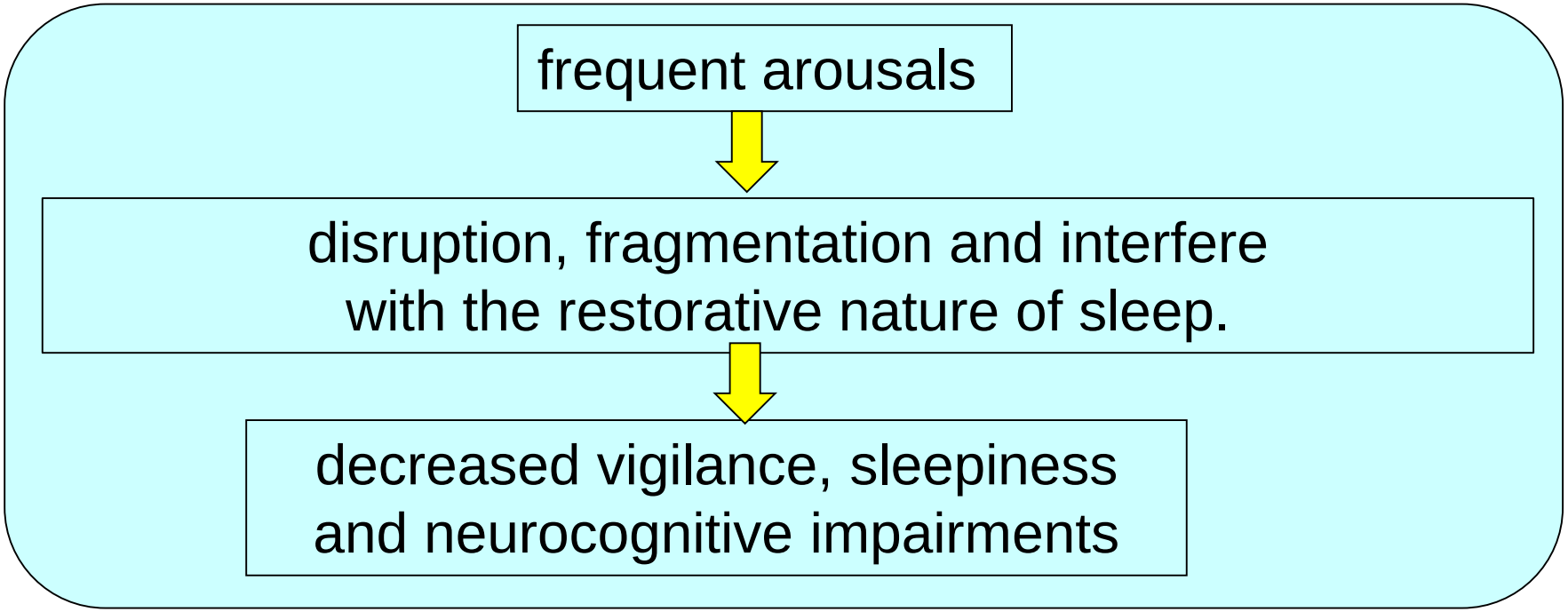
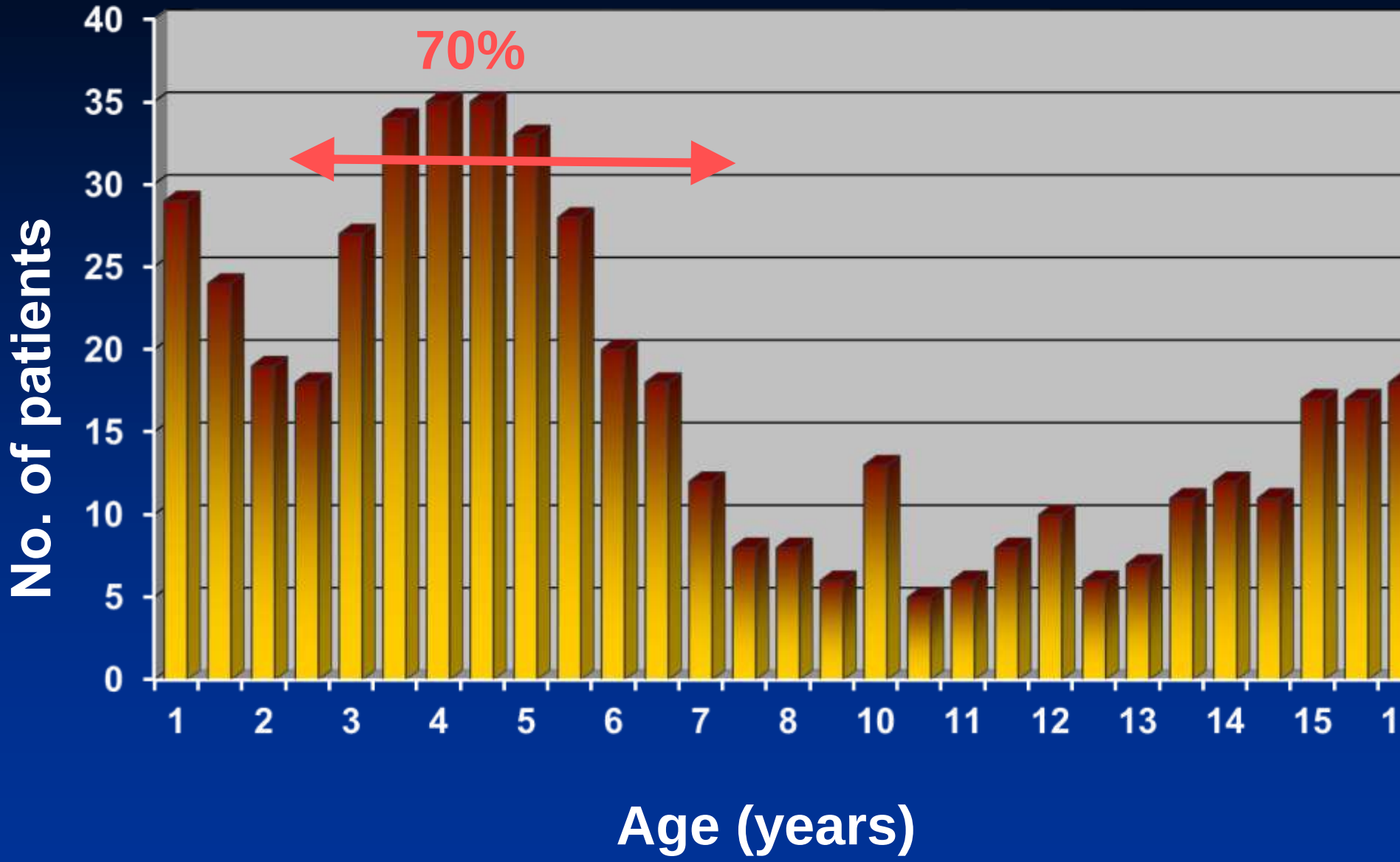
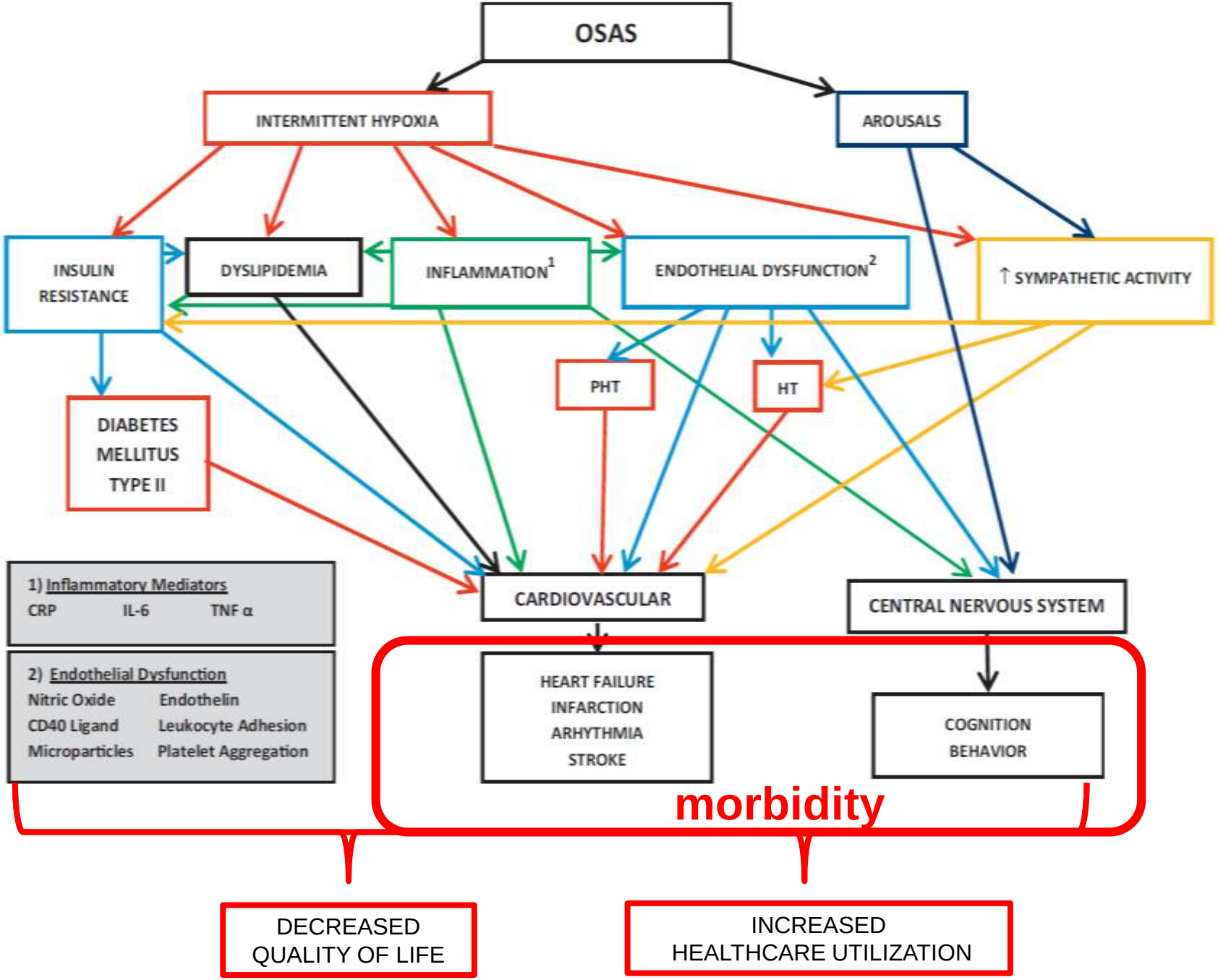


AGE DISTRIBUTION OF OSA IN CHILDREN



MORBIDITY

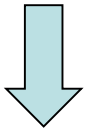

OSAS
INTERMITTENT HYPOXIA
AROUSALS
INSULIN RESISTANCE
DYSLIPIDEMIA
INFLAMMATION[1]
ENDOTHELIAL DYSFUNCTION[2]
↑ SYMPATHETIC ACTIVITY
PHT
HT
DIABETES MELLITUS TYPE II
1) Inflammatory Mediators
CRP IL-6 TNF α
2) Endothelial Dysfunction
Nitric Oxide Endothelin
CD40 Ligand Leukocyte Adhesion
Microparticles Platelet Aggregation
CARDIOVASCULAR
CENTRAL NERVOUS SYSTEM
HEART FAILURE
INFARCTION
ARHYTHMIA
STROKE
COGNITION
BEHAVIOR
morbidity
DECREASED QUALITY OF LIFE
INCREASED HEALTHCARE UTILIZATION

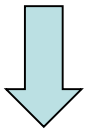
Neurocognitive and neurobehavioral

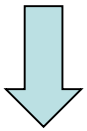
respiratory-related EEG arousals (RERAs)

insufficient sleep duration

intermittent hypoxia and hypercarbia

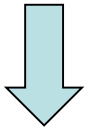






oxidative stress and systemic inflammation

CRP, IL-6, TNF α



adversely affect the prefrontal cortex and hippocampus

Cognitive deficits associated with pediatric SDB

- Learning, memory, and visuospatial skills
- Language, verbal fluency, and phonological skills
- Concept formation, analytic thinking, and verbal and nonverbal comprehension
- School performance and mathematical abilities (recently reported also in PS)
- Executive functions

Neurobehavioral abnormalities in pediatric SDB

Behavior & attention

- ADHD like symptoms and hyperactivity, ODD
- Aggression / impulsiveness
- Abnormal emotional, behaviors, mood, anxiety

Sleepiness

- Daytime hypersomnolence

  (less clinical, more lab – MSLT)

Results of last 10 years studies of cognitive and behavior Pre vs. Post surgical treatment

Most studies showed post treatment improvement of behavior, quality of life, hyperactivity, ADHD, and impulsivity

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

TECHNICAL REPORT

Diagnosis and Management of Childhood Obstructive Sleep Apnea Syndrome

Pediatrics 2012

AAP 2012: "*In developing children, early diagnosis and treatment of pediatric OSAS may improve a child's long-term cognitive and social potential and school performance. The earlier a child is treated for OSAS, the higher the trajectory for academic and, therefore, economic success*".

Obstructive Sleep Apnea Syndrome

"Chronic enlargement of the tonsillar tissue is affection of great importance, and may influence in extraordinary way the mental and bodily development of children…At night, the child's sleep is greatly disturbed, the respirations are loud and snorting and there is sometimes prolonged pauses…"

The snoring child:
" The child responds slowly to questions...impossible to fix attention for long at a time...looks sullen....The influence upon mental development is striking"

William Osler:
The Principles and Practice of Medicine, 1892

cardiovascular

- Hypertension
- Myocardial function
- Endothelial function
- Autonomic regulation

Hypertension in children with OSAS

Higher DBP during sleep and wake in children with AHI of 16 ± 15. Differences in DBP correlated with respiratory events suggesting a causal link (*Marcus et al., 1998, Horne et al., 2011*) [SBP not or mildly increased]

Increased DBP - using ambulatory 24 h BP monitoring in a dose dependent fashion in:
PS, “mild” OSAS (AHI = 1-5), “moderate” OSAS (AHI > 5).

Dose dependent BP dysregulation:

- Increased BP variability
- Reduction of the physiologic nocturnal dipping

Both phenomena are precursors of systemic HT.

(*Amin et al., 2004*)

Cardiac function

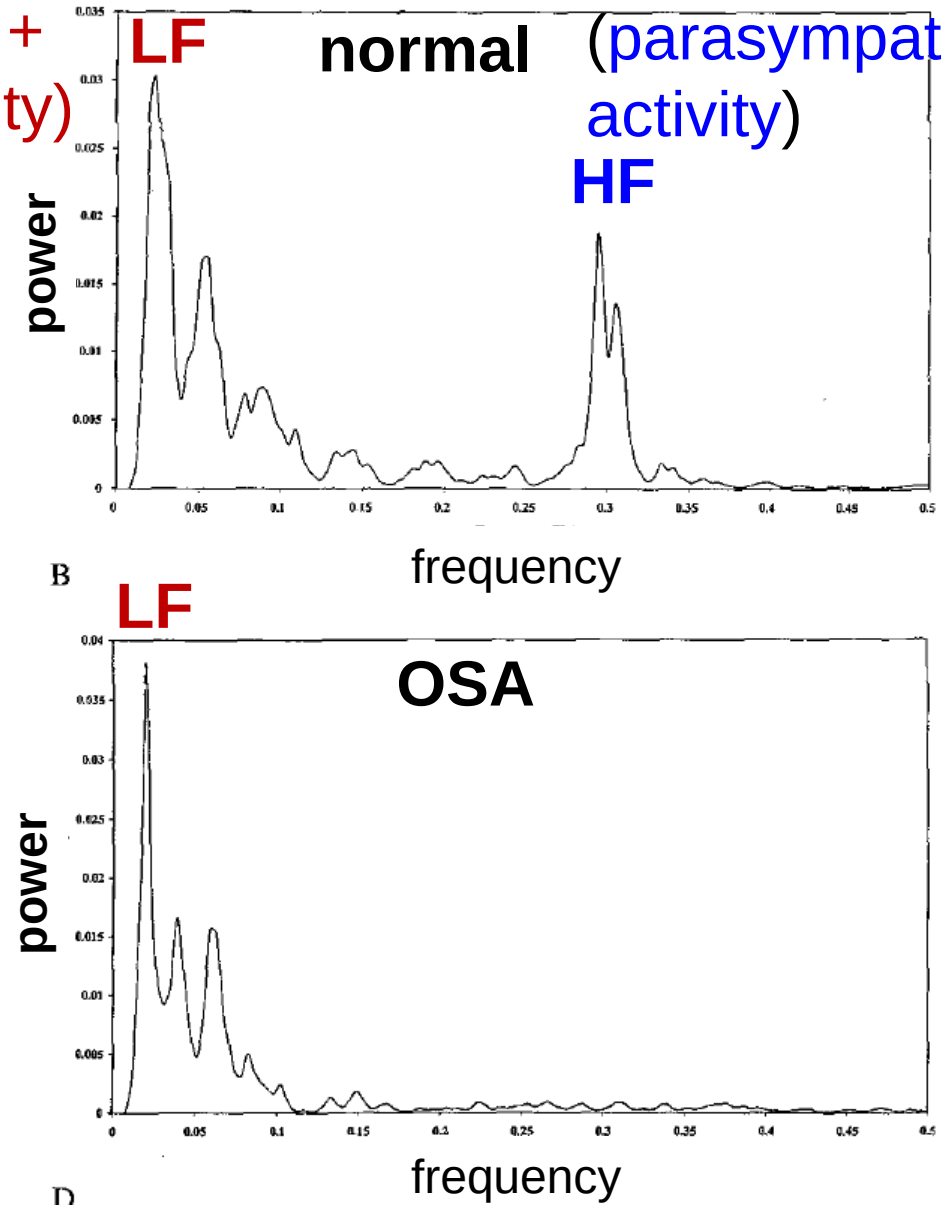
Subtle LV dysfunction and increased mass – OSAS severity (AHI) dependent *(Amin 2005)*

RV dysfunction *(Tal, 1988)*
Pulm. Ht *(Amin, 2005)*

left and right ventricular hypertrophy is significantly associated with postoperative respiratory complications

Autonomic Nervous System 3 techniques

(parasympathethic + sympathethic activity)



HRV

LF/HF band power extracted from ECG by fast Fourier transformation.

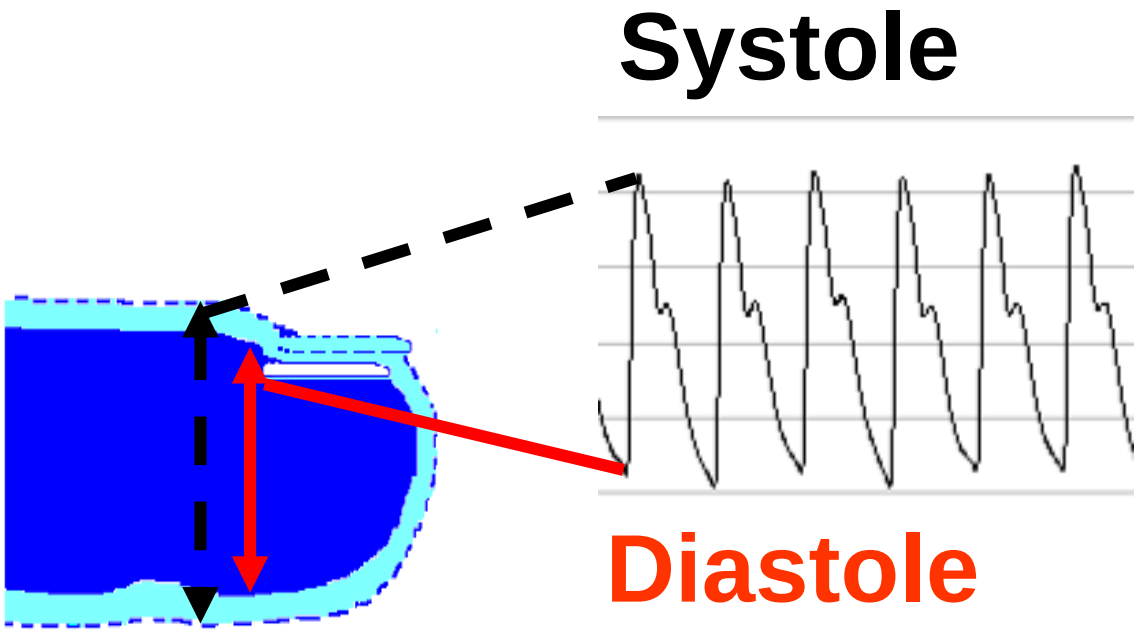
LF/HF is dependent on the balance of sympathetic to parasympathetic activity.

During sleep and awake

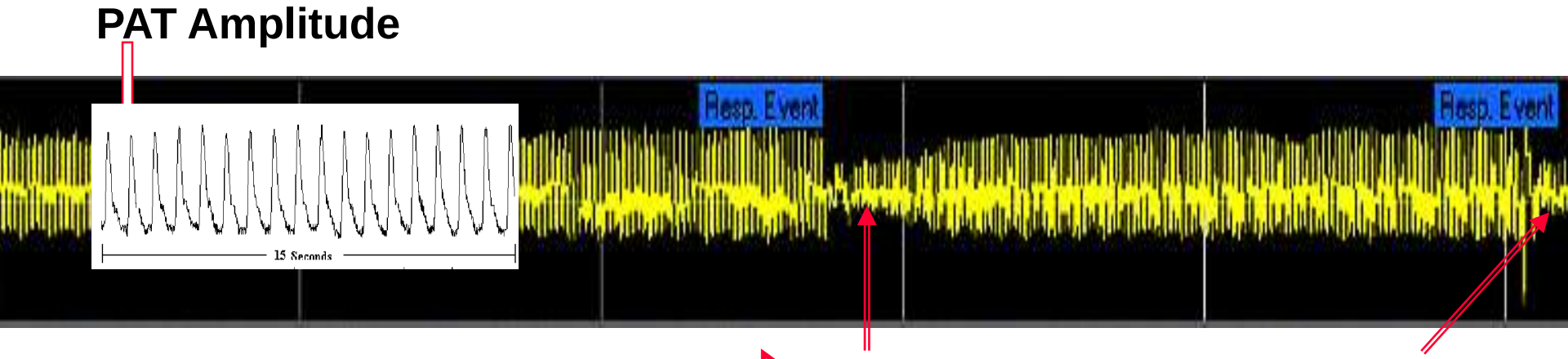
(*Baharav et al.*)

PAT Amplitude = Δ Pulse Volume Change

Pulse arterial tonometry



- ***Measures the arterial volume changes in the fingertip***
- ***A continuous monitoring of the vascular-tone***
- ***Reflection of the sympathetic nervous system***



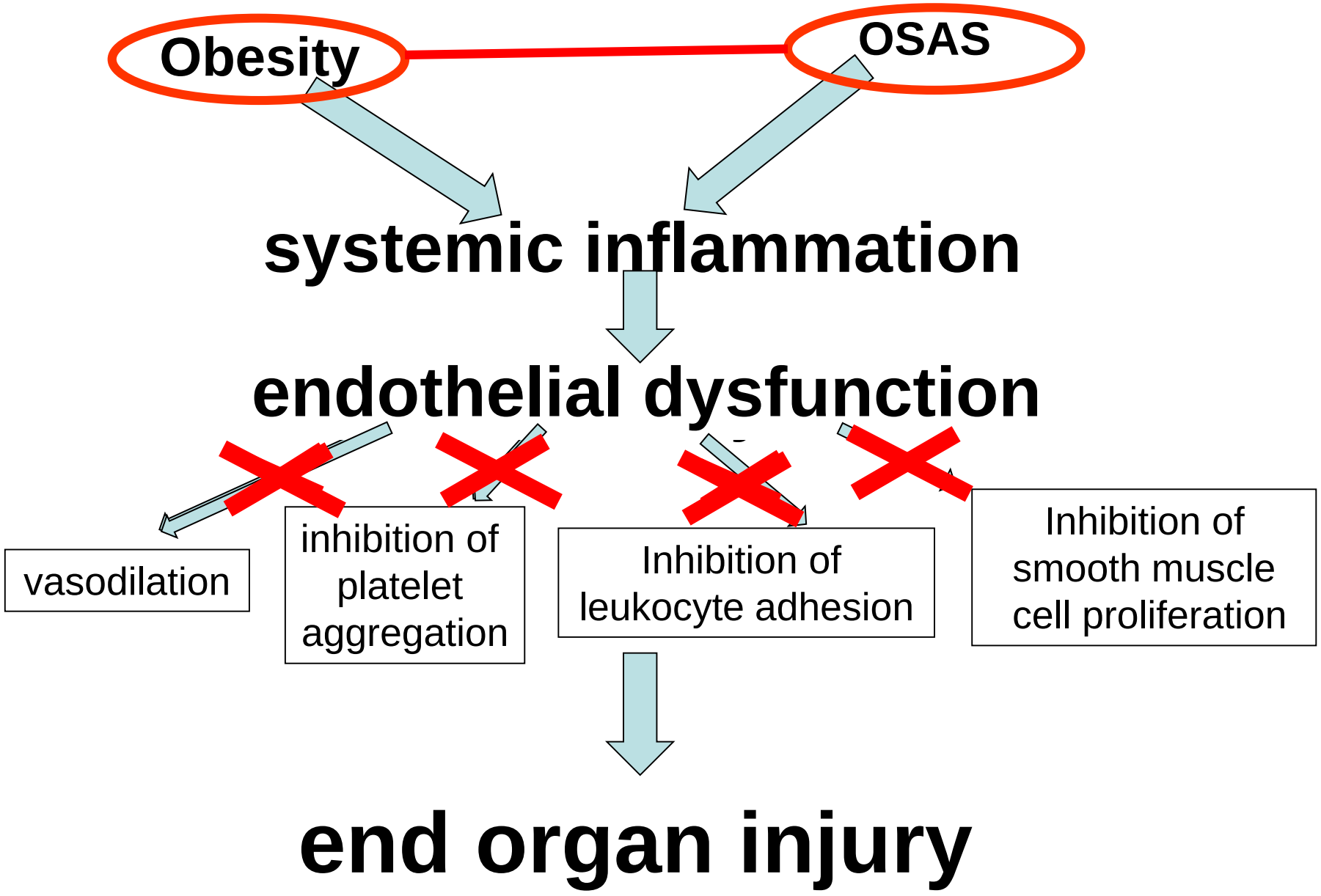
PAT probe → **PAT Signal Attenuation**

α- receptors → **Digital artery vasoconstriction**

Sympathetic activation

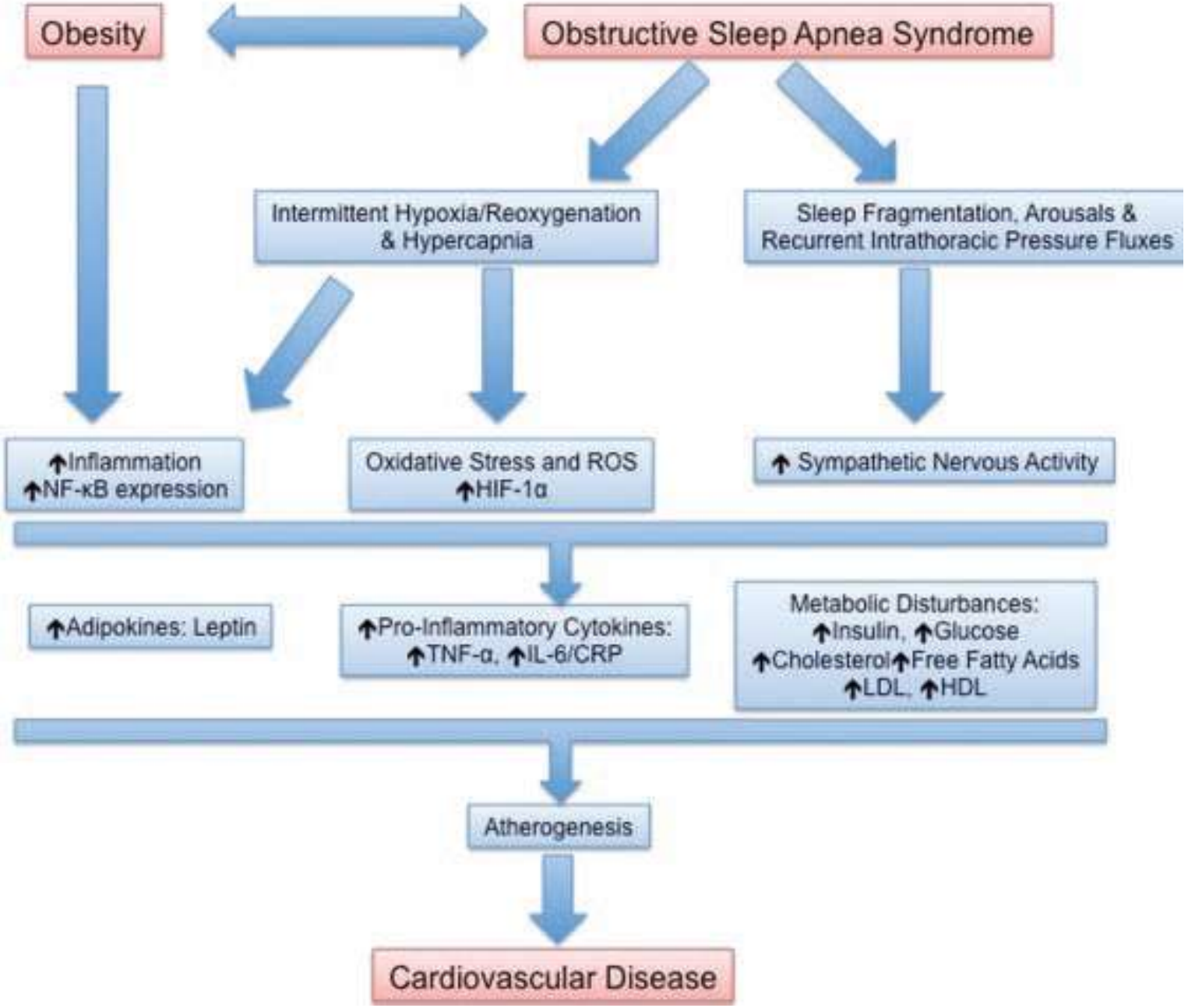
Respiratory event (OSA)

Reperfusion normalized after T&A in 20/26 children (*Gozal et al. 2007)*



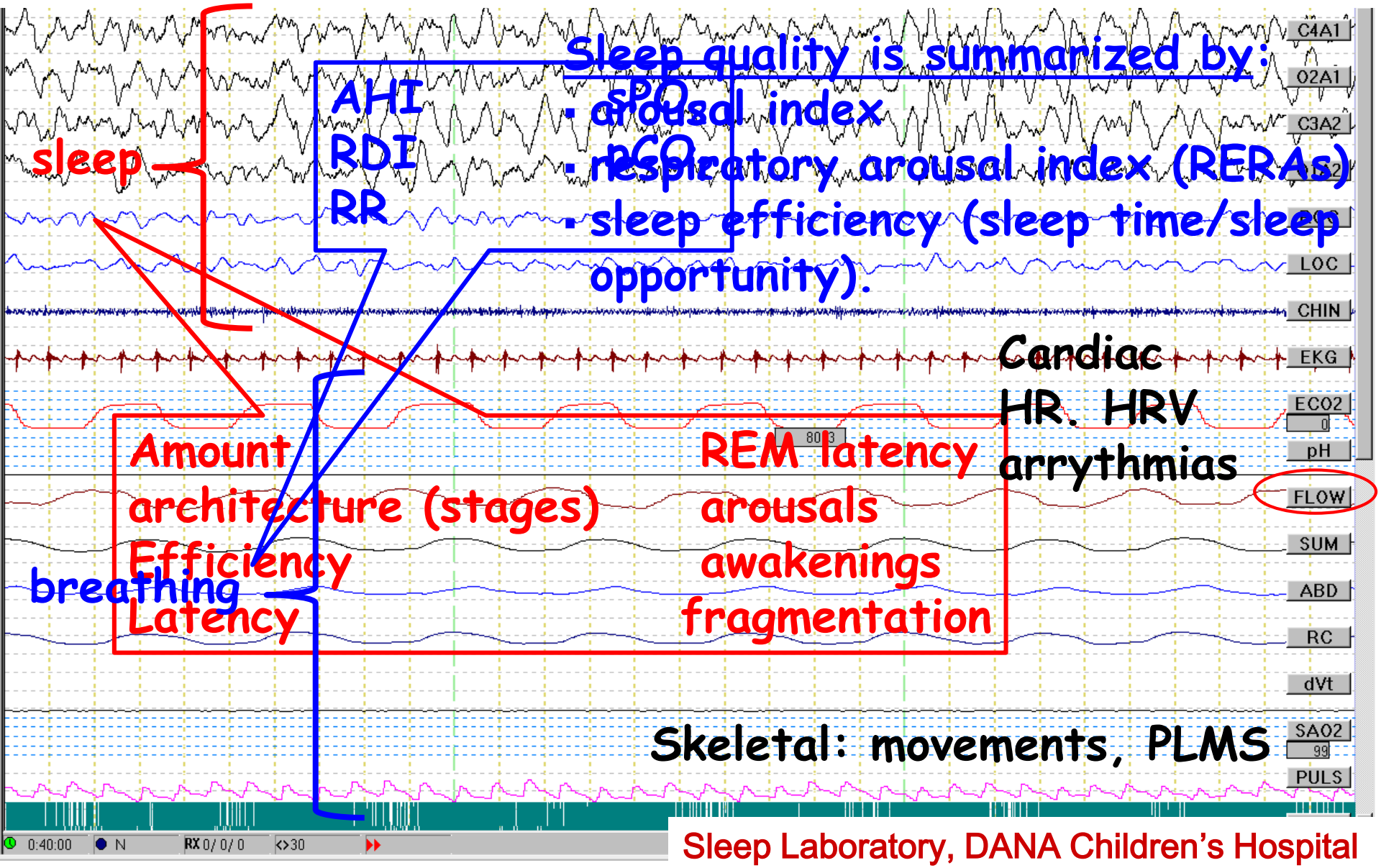
(Lavie and Lavie, 2009)

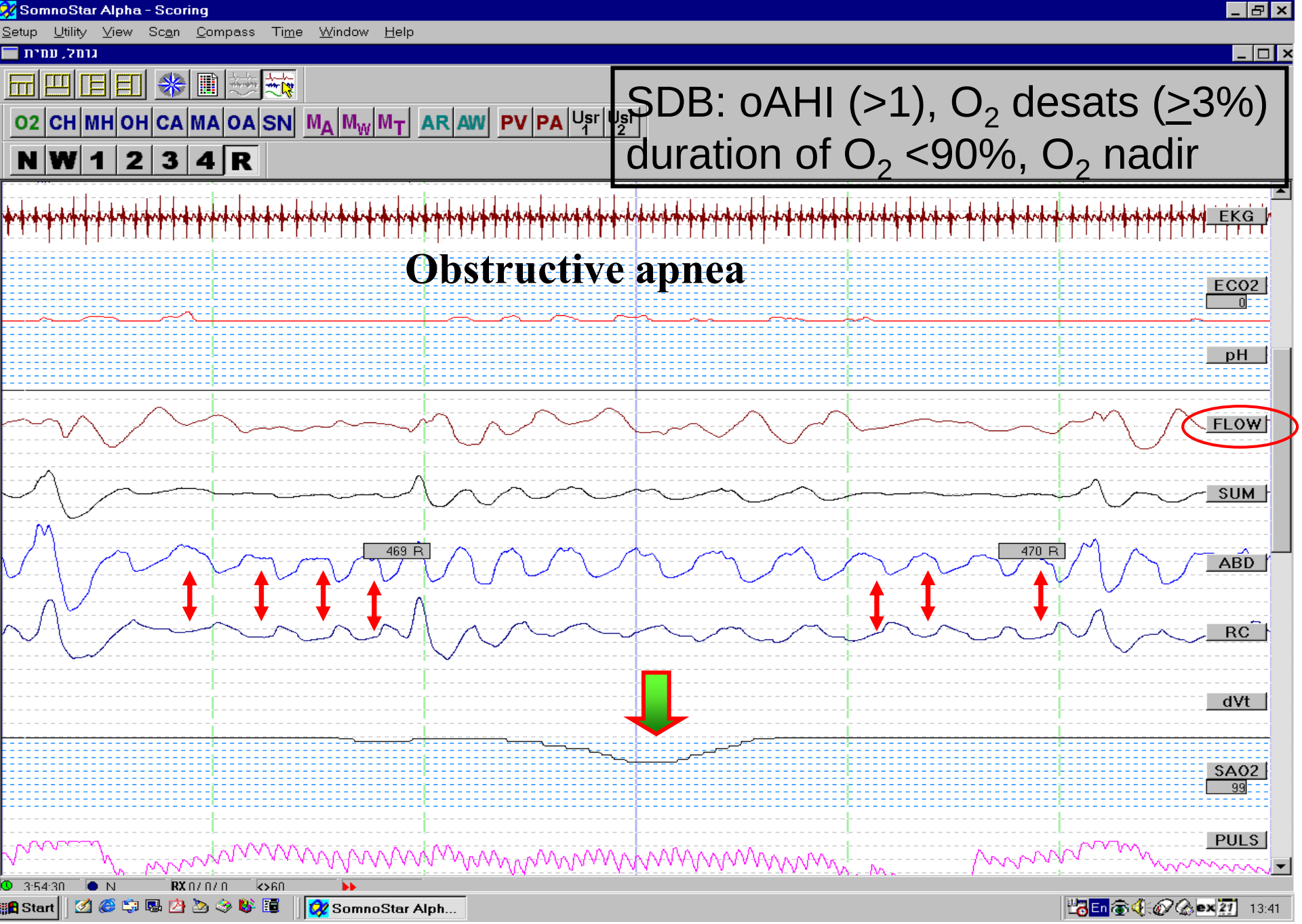
Inflammation


Obesity
Obstructive Sleep Apnea Syndrome
Intermittent Hypoxia/Reoxygenation & Hypercapnia
Sleep Fragmentation, Arousals & Recurrent Intrathoracic Pressure Fluxes
↑Inflammation
↑NF-κB expression
Oxidative Stress and ROS
↑HIF-1α
↑ Sympathetic Nervous Activity
↑Adipokines: Leptin
↑Pro-Inflammatory Cytokines:
↑TNF-α, ↑IL-6/CRP
Metabolic Disturbances:
↑Insulin, ↑Glucose
↑Cholesterol ↑Free Fatty Acids
↑LDL, ↑HDL
Atherogenesis
Cardiovascular Disease

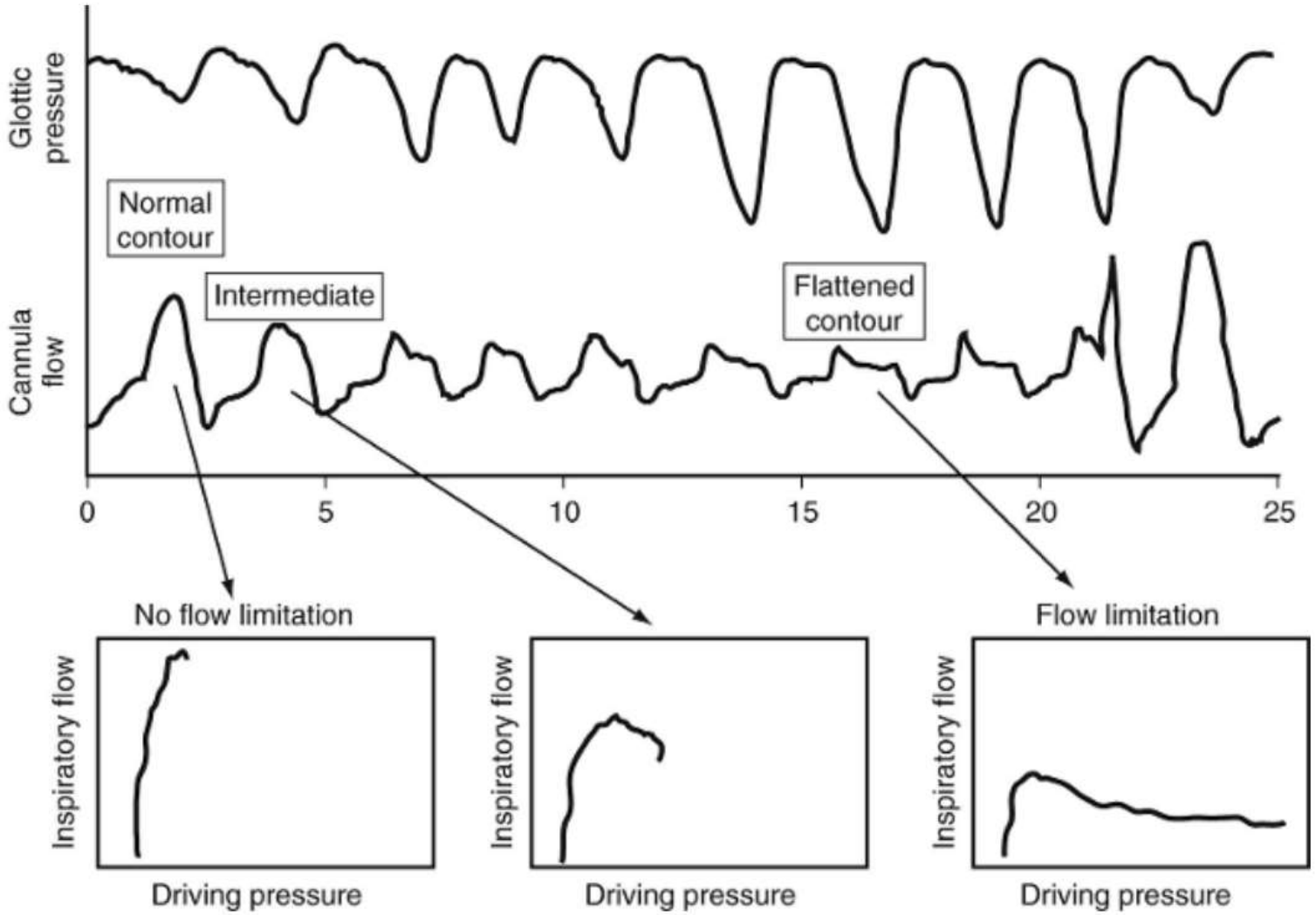
DIAGNOSIS

Polysomnography – gold standard

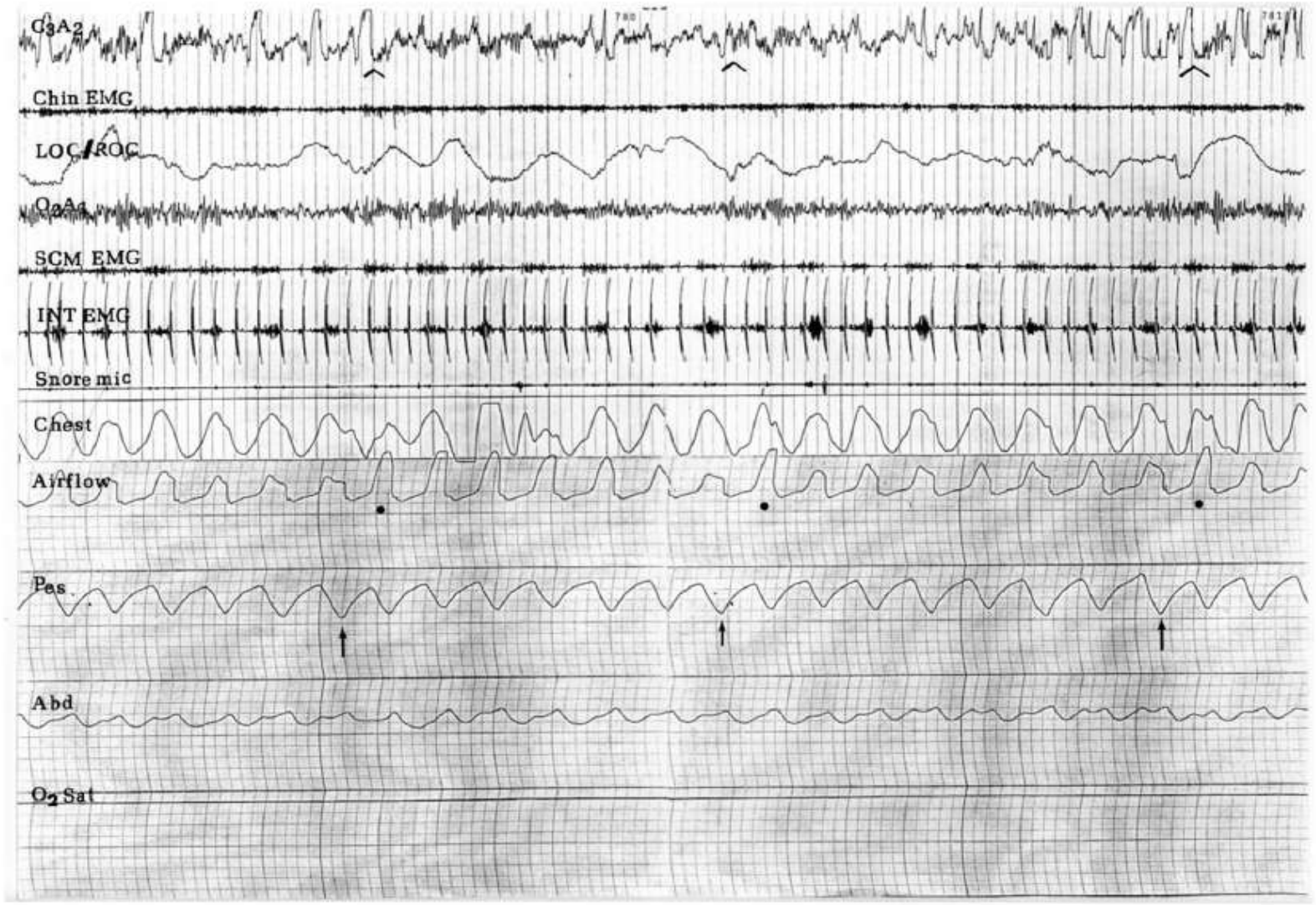




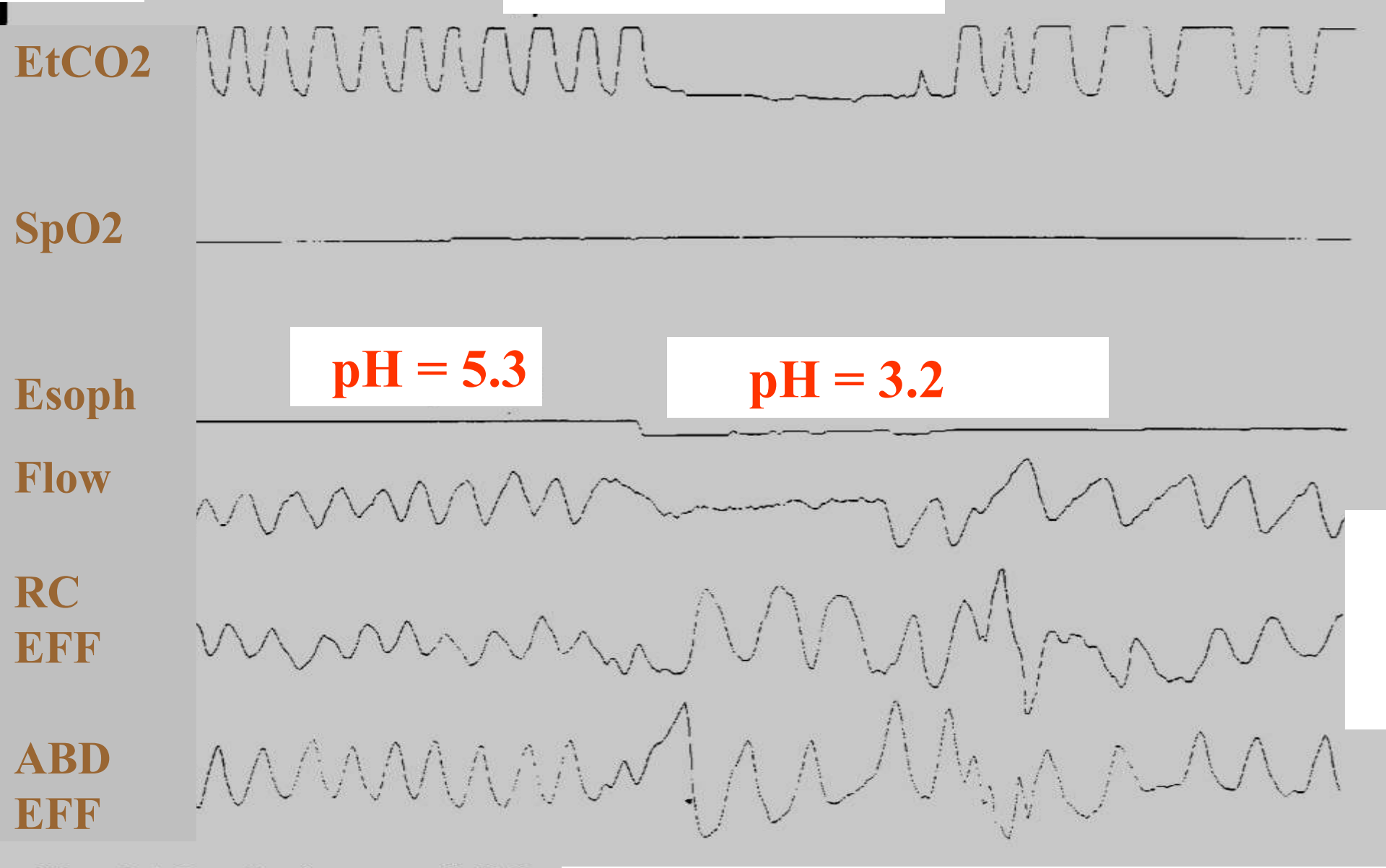
Sleep Laboratory, DANA Children's Hospital


Glottic pressure
Normal contour
Intermediate
Flattened contour
Cannula flow
0
5
10
15
20
25
No flow limitation
Flow limitation
Inspiratory flow
Driving pressure
Inspiratory flow
Driving pressure
Inspiratory flow
Driving pressure

Measurement of flow limitation by nasal pressure



Apnea associated with GER



Sleep Laboratory, DANA Children's Hospital

Limitations of PSG

stressful to children and parents
requires hospitalization
not child's natural environment
not widely available, long waiting
expensive
not correlated with outcome

Is it really a gold standard???

OSAS and Wheezing / ASTHMA

SDB and asthma are inflammatory diseases

potentially have a cumulative effect on morbidity

TABLE 1—Epidemiologic Studies Supporting the Association Between Obstructive Sleep-Disordered Breathing and Recurrent Wheezing/Asthma in Childhood

First author location	Age	No. of subjects	Risk factors	Outcome measure	OR (95% CI)	Ref. n
Corbo; Italy	6–13 y.o.	1,615	Cough and phlegm without cold	Snoring often	1.8 (1.1–3.0)	42
Teculescu; France	5–6.4 y.o.	190	Exercice-induced bronchospasm	Snoring often	8.7 (2.8–26.4) [relative risk]	43
Redline; USA	2–18 y.o.	399	Physician-diagnosed asthma	Apnea–hypopnea index >10 episodes/hr *	3.8 (1.4–10.6)	44
			Occasional wheezing		3.3 (1.2–8.9)	
			Persistent wheezing		7.5 (2.0–27.4)	
Lu; Australia	2–5 y.o.	974	Physician-diagnosed asthma	Snoring ≥4 nights/week in the absence of a cold	2.0 (1.3–3.1)	45
Ersu; Turkey	5–13 y.o.	2,147	History of asthma	Snoring always or frequently	2.0 (1.1–3.6)	46
Valery; Australia	0–17 y.o.	1,650	Ever had wheezing	Snoring >1 night/week over the last 6 months	2.2 (1.4–3.2)	47
			Wheezing in the last 12 months		5.4 (3.6–8.1)	
			Ever had asthma		3.2 (2.2–4.7)	
			Wheezing during or after exercise in the last 12 months		4.7 (2.8–7.8)	
Chng; Singapore	4–7 y.o.	10,279	Physician-diagnosed asthma	Snoring	1.3 (1.1–1.6)	48
Sulit; USA	8–11 y.o.	835	Obstructive apnea–hypopnea index ≥5 episodes/hr or obstructive apnea index ≥1 episode/hr	Wheezing apart from colds in the last year or treatment with asthma medications in the last 3 months	1.9 (1.3–2.9)	53
Desager; Belgium	7–14 y.o.	943	Wheezing in the last 12 months	Snoring in the last 6 months	1.9 (1.0–3.9)	41
Marshall; Australia	5 y.o.	516	Wheezing in the last 12 months and either an asthma diagnosis between 18 months to 5 years or >12% increase in FEV1 after a bronchodilator	Snoring	2.7 (1.2–5.9)	49
				Snoring ≥3 nights/week	3.4 (1.6–7.2)	
Verhulst; Sri Lanka	6–12 y.o.	652	Wheezing in the last 12 months	Snoring	2.8 (1.6–4.7)	50
Kuehni; UK	1–5 y.o.	6,811	1–10 attacks of wheeze	Snoring almost always over the last 12 months	1.4 (1.1–1.7)	51
			>10 attacks of wheeze		2.6 (1.5–4.7)	
Kaditis; Greece	Children ≥2 y.o.	442	Physician-diagnosed wheezing requiring treatment in the past 12 months	Snoring ≥1 night/week over the last 6 months	1.7 (1.1–2.7)	52

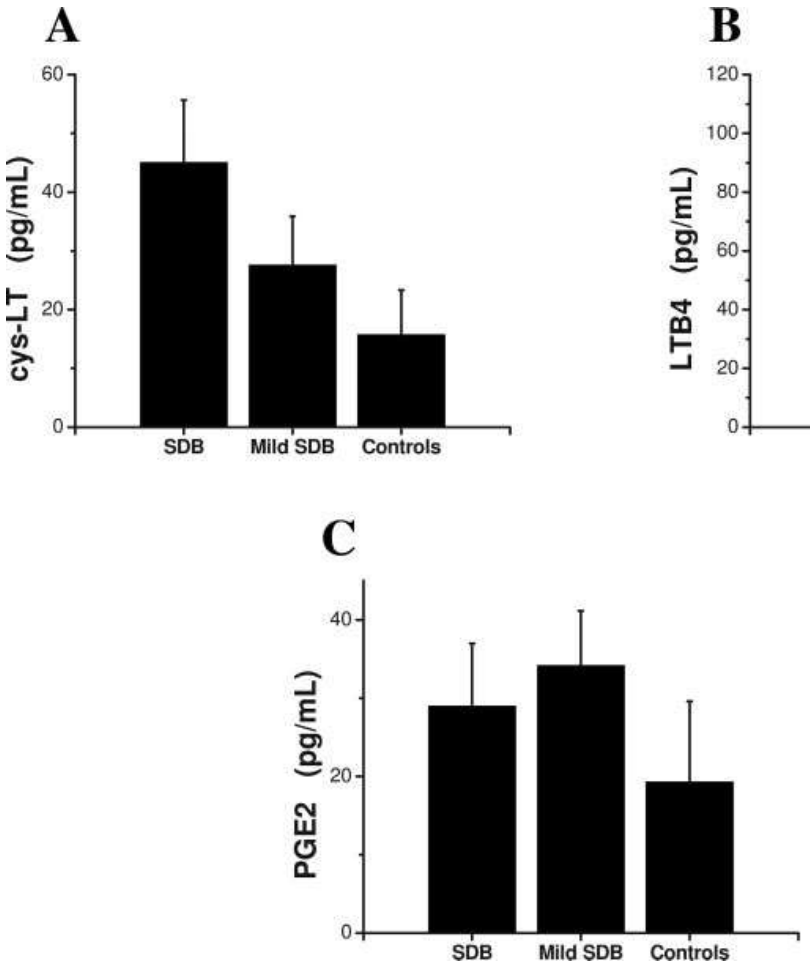
Increase rate of snoring and elevated AHI in children with history of wheezing and asthma (“dose-dependent”)

Total n > 2,500 children. Most studies are based mainly on questionnaires

* Objective data using PSG

PATHOGENETIC LINKS BETWEEN OBSTRUCTIVE SDB AND RECURRENT WHEEZING/ASTHMA

Airway inflammation related to leukotrienes and airway oxidative stress are possibly implicated in the pathogenesis of both disorders.



Goldbart A, Chest 2006
(Kaditis 2011)

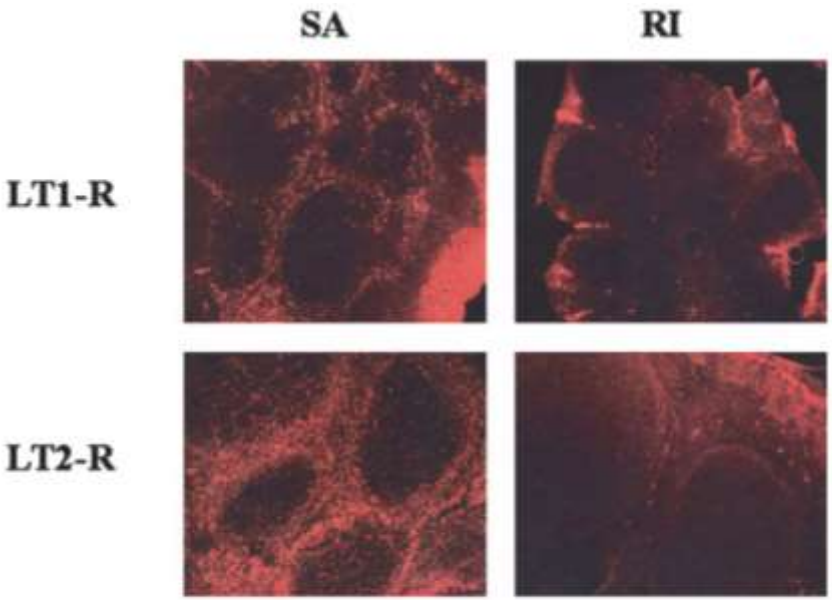
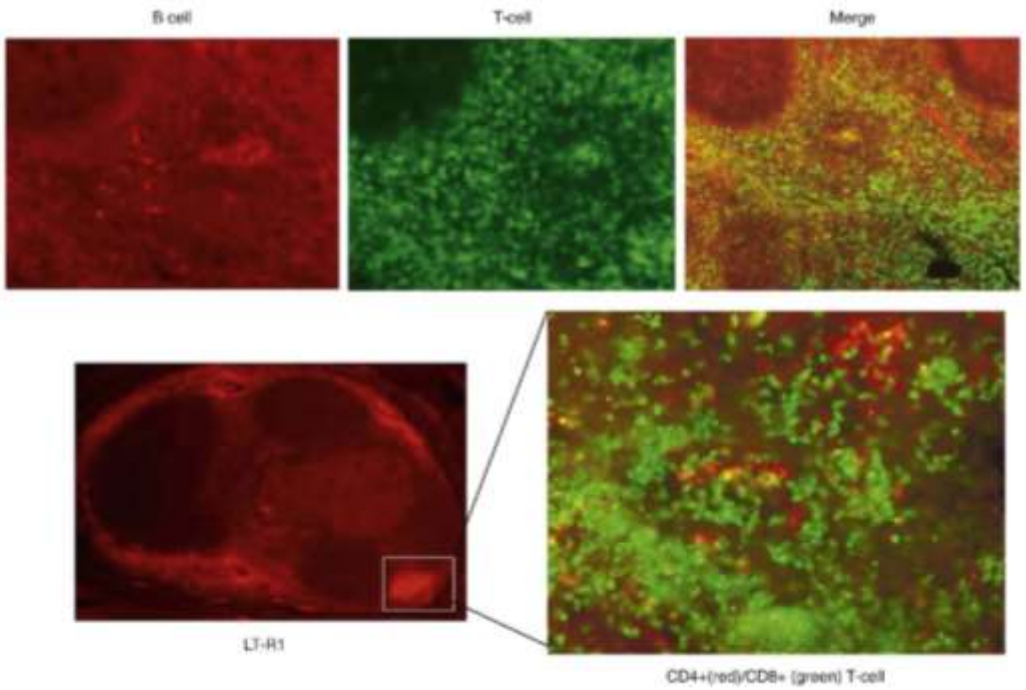


FIGURE 2. : Representative immunohistochemical assessment for LT1-R and LT2-R in a tonsil from a patient with SA and in one patient with RIs. A higher abundance of LT-Rs is apparent in the SA patient as well as a different topographic distribution of the LT-Rs. Similar findings occurred in five sets of tonsils examined for each of the two patient categories.

Goldbart A, 2004



LKG, Ped Pulm 2011

Increased expression of cysteinyl leukotrienes and their receptors within the pharyngeal lymphoid tissues contributes to adenotonsillar hypertrophy and severity of SDB.

TABLE 3—Changes in Asthma Symptoms and Control in Poorly Controlled Asthmatic Children With OSA Before and After T&A, and in Those Without OSA Before and After Sleep Studies

	OSA (+), n = 35			OSA (−), n = 24			P-Value (OSA (+) vs. OSA (−))
	Pre-T&A	Post-T&A	*P*-Value	Pre-NPSG	Post-NPSG	*P*-Value	
Acute asthma exacerbations (/year)	4.1 ± 1.3	1.8 ± 1.4	<0.0001	3.5 ± 1.5	3.7 ± 1.7	NS	<0.0001
Weekly β-agonist rescue use (/week)	4.3 ± 1.8	2.1 ± 1.5	<0.001	4.2 ± 1.9	3.9 ± 2.2	NS	<0.001
Asthma symptom score	3.1 ± 1.9	1.9 ± 1.7	<0.0001	3.2 ± 2.0	3.1 ± 2.1	NS	<0.001
FEV_1 (% predicted)	80.1 ± 8.7[1]	86.5 ± 8.4	<0.04	82.5 ± 9.1[2]	83.1 ± 9.7	NS	0.05

[1]n = 18.
[2]n = 12.

- 92 children with poorly-controlled asthma (3-10 y.)
- OSA = 63% (AHI >5 by PSG), OR = 40.1
- T&A in 35
- No T&A in 24 (controls)
- Follow-up – 1 year

LKG, Ped Pulm 2011

Adenotonsillectomy Outcomes in Treatment of Obstructive Sleep Apnea in Children

A Multicenter Retrospective Study

Rakesh Bhattacharjee[1*], Leila Kheirandish-Gozal[1,9], Karen Spruyt[1,9], Ron B. Mitchell[2], Jungrak Promchiarak[3], Narong Simakajornboon[3], Athanasios G. Kaditis[4], Deborah Splaingard[5], Mark Splaingard[5], Lee J. Brooks[6], Carole L. Marcus[6], Sanghun Sin[7], Raanan Arens[7], Stijn L. Verhulst[8], and David Gozal[1,9]

623 Children from 8 Centers

n= 251 Kosair Children's Hospital, Louisville, KY
n= 112 Cardinal Glennon Children's Hospital, Saint Louisville, MO
n= 80Cincinnati Childrens Hospital, Cinncinnati, OH
n= 70 Larissa University Hospital, Columbus, OH
n= 44 Nationwide Children's Hospital, Columbus, OH
n= 23 Children's Hospital fo Philadelphia, PA
n= 23 Montefiore Medical Center, Bronx, NY
n= 20 Antwerp University Hospital, Wilrijk, Belgium

-3 subjects
Incomplete PSG Data

620 Children

-18 subjects
Repeat PSG < 40d
Repeat PSG > 720d

602 Children

- 24 subjects
12 subject with Down's
1 subject w/ Achondroplasia
1 subject w/ Prader Willi
1 subject w/ Trisomy 17
1 subject w/ Turners
1 subject w/ Goldenhar
1 subject with Neurofibromatosis
1 subject w/ Tuberous Sclerosis
1 subject w/ Chromosomal anomoly
4 subjects w/ previous T&A

578 Children

AJRCCM 2010

A multicenter, retrospective review of children who underwent polysomnography before and after T&A. The presence of asthma was a significant predictor of residual SDB in non-obese subjects.

TABLE 5. INFLUENCE OF DEMOGRAPHIC FACTORS IN NONOBESE CHILDREN

	Wald Statistic	*P* Value
Age	4,870	<0.001
Body mass index z-score	315	<0.001
Asthma	8	0.006
Preadenotonsillectomy apnea-hypopnea index	6	0.015

Body mass index z-score ≤1.65.

Bhattacharjee R, AJRCCM 2010

Outcome of T&A for OSAS

TABLE 2. POLYSOMNOGRAPHIC DATA IN ALL CHILDREN UNDERGOING ADENOTONSILLECTOMY FOR OBSTRUCTIVE SLEEP APNEA SYNDROME

Variable	Preadenotonsillectomy	Postadenotonsillectomy	*P* Value
Sleep efficiency, % (n = 397)	83.8 ± 11.2	85.5 ± 11	<0.001
Sleep onset latency, min (n = 393)	29.8 ± 38.3	27.4 ± 33.9	= 0.264
Number of awakenings, no. (n = 300)	12.9 ± 11	10.6 ± 8.2	<0.001
Wake after sleep onset, % of TST (n = 397)	13.4 ± 37.7	9.2 ± 11	= 0.113
REM onset latency, min (n = 371)	157.6 ± 97	155.7 ± 80.5	= 0.719
Stage 1 sleep, % of TST (n = 394)	6.8 ± 8	5.6 ± 5.2	= 0.002
Stage 2 sleep, % of TST (n = 394)	43.3 ± 12.5	45.8 ± 27.3	= 0.075
Stage 3 sleep, % of TST (n = 394)	7.8 ± 7.2	8.5 ± 11.2	= 0.151
Stage 4 sleep, % of TST (n = 394)	20.5 ± 9.9	21.5 ± 11.7	= 0.134
Stage REM sleep, % of TST (n = 507)	16.6 ± 7.4	16.8 ± 7.1	= 0.380
Total no. of obstructive hypopneas (n = 408)	90.7 ± 100.3	25.5 ± 38.8	<0.001
Total no. of obstructive apneas (n = 408)	37.9 ± 69.2	5.8 ± 20	<0.001
Apnea-hypopnea index, events/h TST (n = 578)	18.2 ± 21.4	4.1 ± 6.4	<0.001
Obstructive apnea index, events/h TST (n = 476)	6 ± 10.3	1.3 ± 4.4	<0.001
Total apnea index, events/h TST (n = 420)	6.7 ± 10.7	1.6 ± 3.3	<0.001
Respiratory arousal index, events/h TST (n = 173)	7.7 ± 8.1	2.4 ± 3	<0.001
Total arousal index, events/h TST (n = 285)	14.8 ± 16.2	9.8 ± 6	<0.001
Oxygen saturation nadir, % (n = 493)	80.2 ± 13.1	86.2 ± 8.3	<0.001

T&A resulted in a reduction in AHI in 91% of children
Only 27.2% normalized their AHI (<1)
50% were obese

Bhattacharjee et al. 2010

Residual OSAS = up to 27% (*Tauman et al. J Pediatr 2006*)
Residual OSAS (by PSQ): = 15% (*Sivan et al. ATS 2014)*

Childhood Adenotonsillectomy Trial (CHAT)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized Trial of Adenotonsillectomy for Childhood Sleep Apnea

Carole L. Marcus, M.B., B.Ch., Reneé H. Moore, Ph.D., Carol L. Rosen, M.D., Bruno Giordani, Ph.D., Susan L. Garetz, M.D., H. Gerry Taylor, Ph.D., Ron B. Mitchell, M.D., Raouf Amin, M.D., Eliot S. Katz, M.D., Raanan Arens, M.D., Shalini Paruthi, M.D., Hiren Muzumdar, M.D., David Gozal, M.D., Nina Hattiangadi Thomas, Ph.D., Janice Ware, Ph.D., Dean Beebe, Ph.D., Karen Snyder, M.S., Lisa Elden, M.D., Robert C. Sprecher, M.D., Paul Willging, M.D., Dwight Jones, M.D., John P. Bent, M.D., Timothy Hoban, M.D., Ronald D. Chervin, M.D., Susan S. Ellenberg, Ph.D., and Susan Redline, M.D., M.P.H., for the Childhood Adenotonsillectomy Trial (CHAT)

2013

Aim: to evaluate the efficacy of early T&A versus watchful waiting with respect to **cognitive**, **behavioral**, **quality-of-life**, and **sleep** factors.

The primary outcome was a neurobehavioral measure of **attention and executive function**, a domain that has been shown to be sensitive to intermittent hypoxemia related to the OSAS.

Selection criteria:

In	**Out**
Age: 5-9 years	AHI>30 or OAI>20
AHI $\geq$ 2 or OAHI $\geq$ 1	spO_2 < 90% for >2% TST
	BMI z score > 3

Outcome assessment at baseline and 7 m. post randomization

PSG
cognitive and behavioral testing

- **NEPSY** (Developmental Neuropsychological Assessment - scores range 50 to 150 [100 representing the population mean])
- **Conners'** (caregiver and teacher ratings of behavior)
- **BRIEF** (summary measures of behavioral regulation and metacognition)
- **PSQ-SRBD** (pediatric sleep questionnaire for SDB)
- **Epworth sleepiness score**
- **PedsQL** (Pediatric Quality of Life Inventory)

1.2008-9.2011

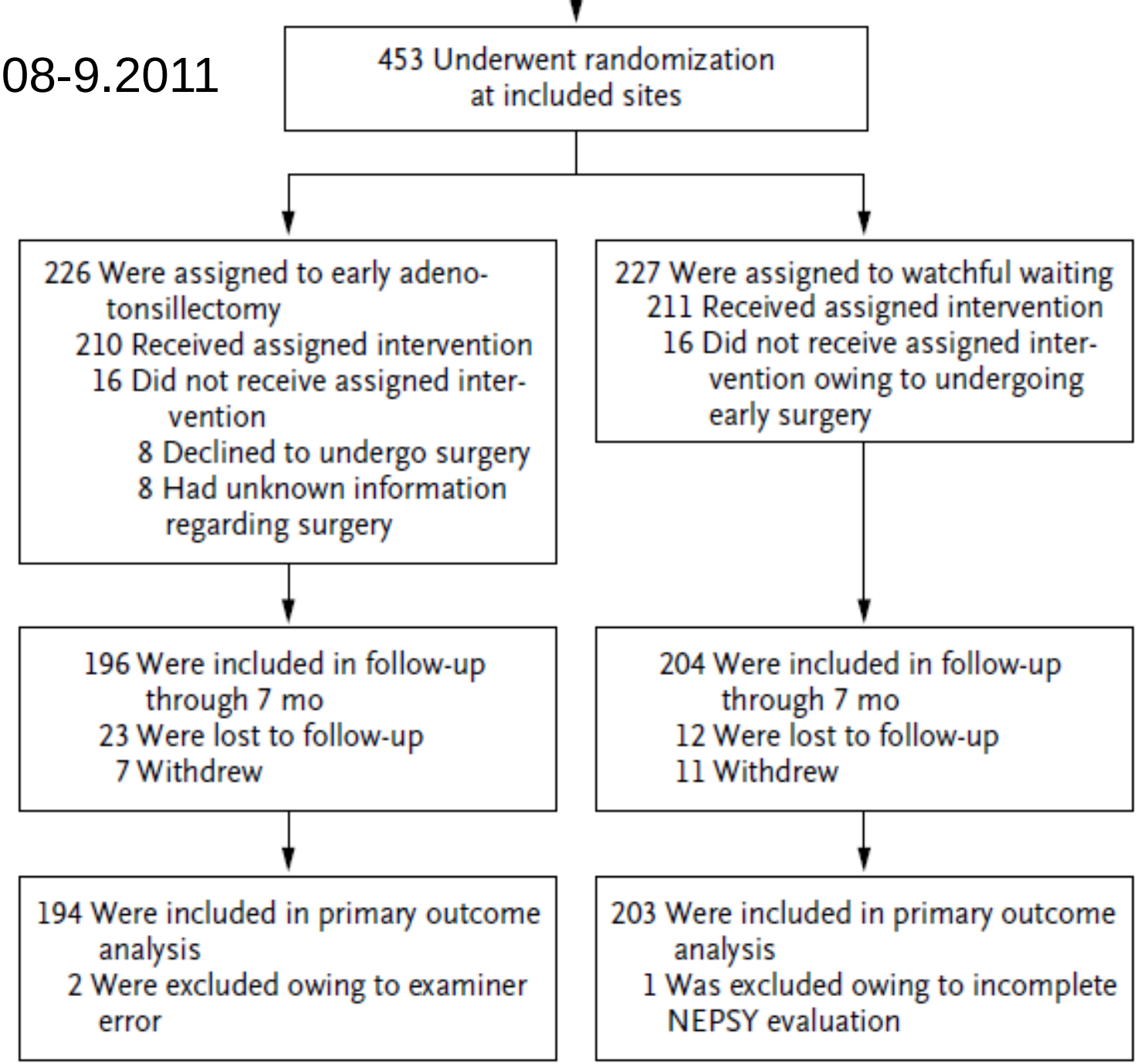

453 Underwent randomization at included sites
226 Were assigned to early adenotonsillectomy
210 Received assigned intervention
16 Did not receive assigned intervention
8 Declined to undergo surgery
8 Had unknown information regarding surgery
227 Were assigned to watchful waiting
211 Received assigned intervention
16 Did not receive assigned intervention owing to undergoing early surgery
196 Were included in follow-up through 7 mo
23 Were lost to follow-up
7 Withdrew
204 Were included in follow-up through 7 mo
12 Were lost to follow-up
11 Withdrew
194 Were included in primary outcome analysis
2 Were excluded owing to examiner error
203 Were included in primary outcome analysis
1 Was excluded owing to incomplete NEPSY evaluation

Table 2. Outcome Measures.*

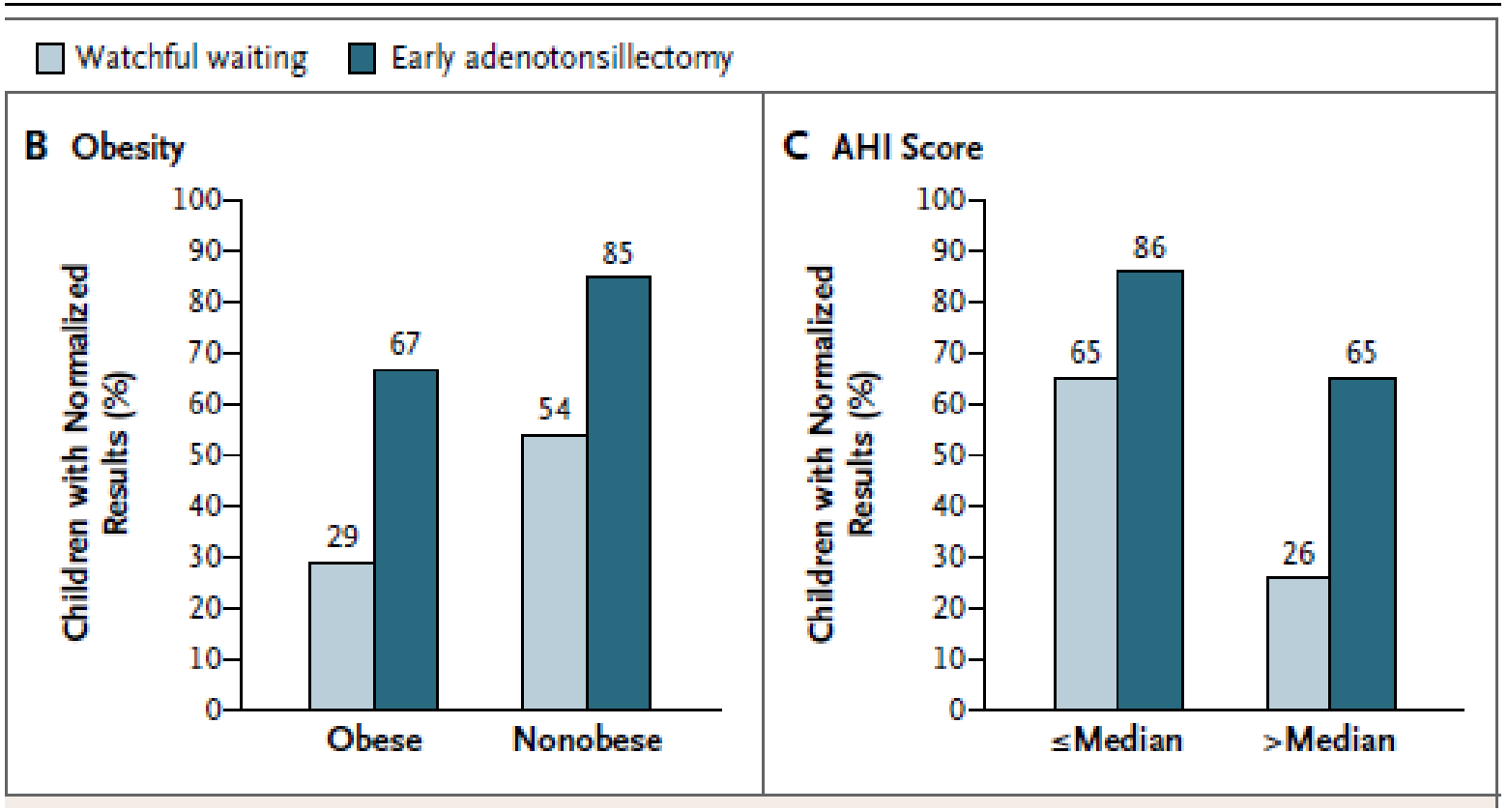
Outcome	Normative Mean	Watchful Waiting		Early Adenotonsillectomy		Effect Size†	P Value
		Baseline	Change from Baseline to 7 Mo	Baseline	Change from Baseline to 7 Mo		
Primary outcome							
NEPSY attention and executive-function score‡	100±15	101.1±14.6	5.1±13.4	101.5±15.9	7.1±13.9	0.15	0.16
Secondary outcomes							
Conners' Rating Scale score§	50±10						
Caregiver rating		52.6±11.7	−0.2±9.4	52.5±11.6	−2.9±9.9	0.28	0.01
Teacher rating		55.1±12.8	−1.5±10.7	56.4±14.4	−4.9±12.9	0.29	0.04
BRIEF score¶	50±10						
Caregiver rating		50.1±11.5	0.4±8.8	50.1±11.2	−3.3±8.5	0.28	<0.001
Teacher rating		56.4±11.7	−1.0±11.2	57.2±14.1	−3.1±12.6	0.18	0.22
PSQ-SRBD score‖	0.2±0.1	0.5±0.2	−0.0±0.2	0.5±0.2	−0.3±0.2	1.50	<0.001
PedsQL score**	78±16	76.5±15.7	0.9±13.3	77.3±15.3	5.9±13.6	0.37	<0.001
Apnea–hypopnea index — no. of events/hr††	NA						
Median		4.5	−1.6	4.8	−3.5	0.57	<0.001‡‡
Interquartile range		2.5 to 8.9	−3.7 to 0.5	2.7 to 8.8	−7.1 to −1.8		

NEPSY-Developmental Neuropsychological Assessment

Conners' - caregiver and teacher ratings of behavior (

BRIEF - summary measures of behavioral regulation and metacognition

Figure 2. Normalization of Polysomnographic Findings.



obese - BMI ≥ 95th percentile

- **Median AHI**
- **WW = 4.5**
- **T&A = 4.8**

CHAT study summary

surgery resulted in greater improvement in:

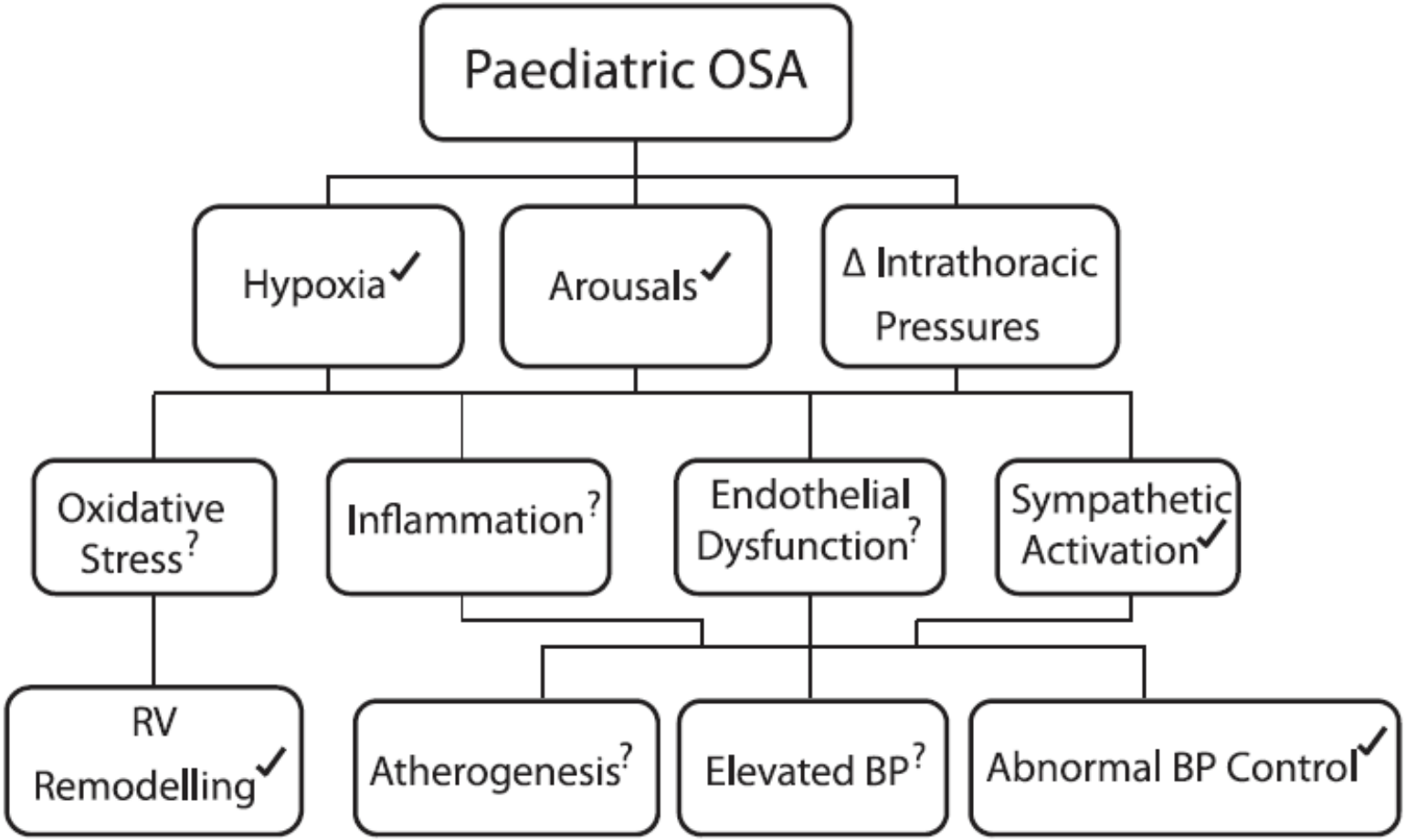
- Symptoms
- Behavior
- Quality of life
- Polysomnographic findings

no greater improvement in attention and executive functions

CHAT study limitations

- Age – 5-9 years
- Mild-moderate cases (median AHI<5), therefore, baseline functions were within normal range, hence improvement was mild.
- No A group

The effects of treatment on the cardiovascular consequences of OSA in children



✓ studies that show improvement in the cardiovascular outcome with treatment
✓ ? Conflicting results

TREATMENT OPTIONS

- ✓ **Surgical**
- ✓ **Mechanical**
- ✓ **Medications**

19.2.2015

ynet
ידיעות אחרונות

חדשות בריאות

בת שש נפטרה לאחר ניתוח להסרת שקדים

הילדה נותחה להסרת שקדים ושוחררה לביתה במצב טוב. לאחר יומיים החלה לסבול מדימום והובהלה על ידי הוריה לבית החולים, שם נקבע מותה. ביה"ח כרמל: "הילדה נכנסה לסטטיסטיקה מצערת"

סיבוך נדיר כתוצאה מניתוח להוצאת השקדים גרם למותה של ילדה מירושלים

בת 4 מתה אחרי ניתוח שקדים

...רת השקדים בבית־החולים „משגב לדך" בירושלים ושוחררה לביתה במצב טוב ...אחרה מוקדמים, פרץ לפתע זרם דם מגרונה ● עד שהגיעה לחדר המיון כבר ...ם הצליחו להחזיק אותה בחיים באופן זמני, אך בלילה הידרדר מצבה עד מוות

„הרופא הרג את אמא"

מירי בלייש (28) שמצבה הסתבך לפני שבועיים בעקבות ניתוח שקרים – נפטרה אתמול ● בנה רניאל (7): „התפללנו, אבל אפילו אלוהים כבר לא יכול היה לתקן את מה שעשו לאמא"

מאת **נואל בנו,**
כתב „ידיעות אחרונות"

OAI

12 weeks

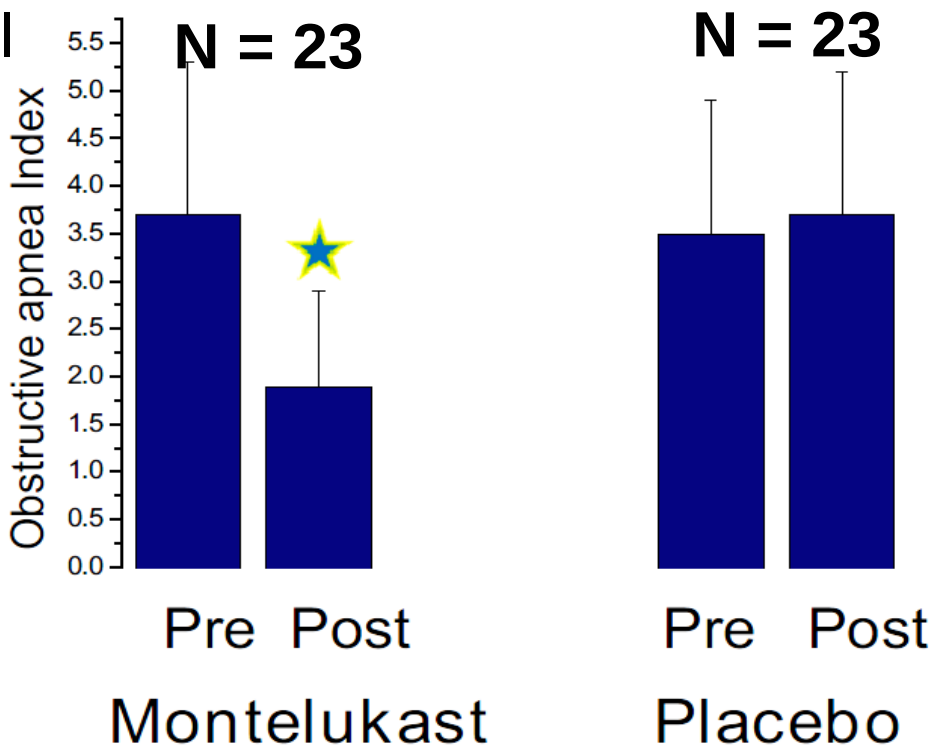


FIGURE 1

Montelukast treatment resulted in a significant improvement in the OAI. The pretreatment average of 3.7 ± 1.6 before (pre) dropped to 1.9 ± 1.0 after (post) treatment; $P < .05$. In contrast, 12 weeks of placebo treatment did not significantly change the OAI; means: 3.5 ± 1.6 (pre) vs 3.7 ± 1.0 (post) treatment; $P = .75$. Star indicates a significant difference between pre and post values.

AHI - no sig. change (p = 0.07)
OAI – did not normalize (no “cure”)
Destauration index - no sig. change (p = 0.09)
Mild OSA, minor change

Goldbart & Tal, Pediatrics 2012

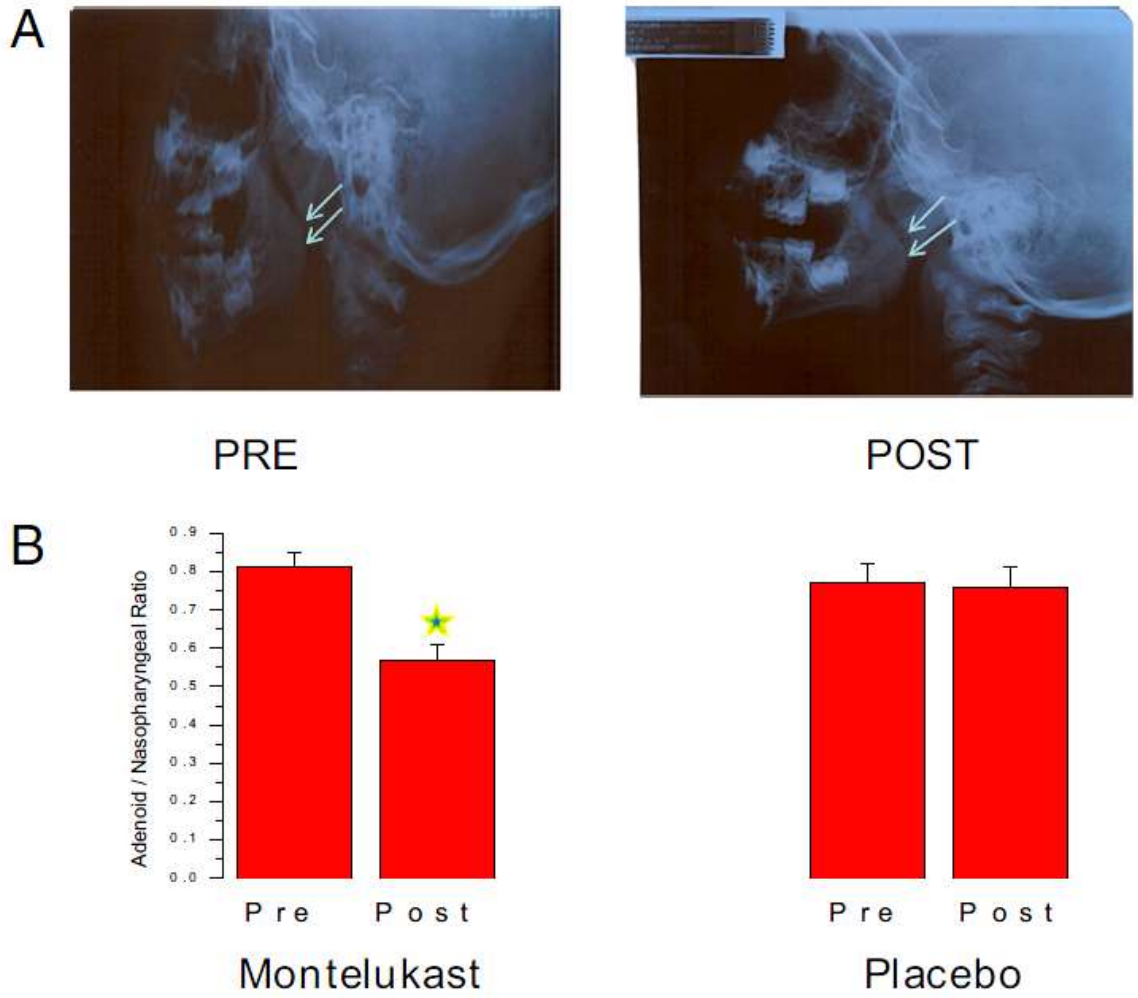
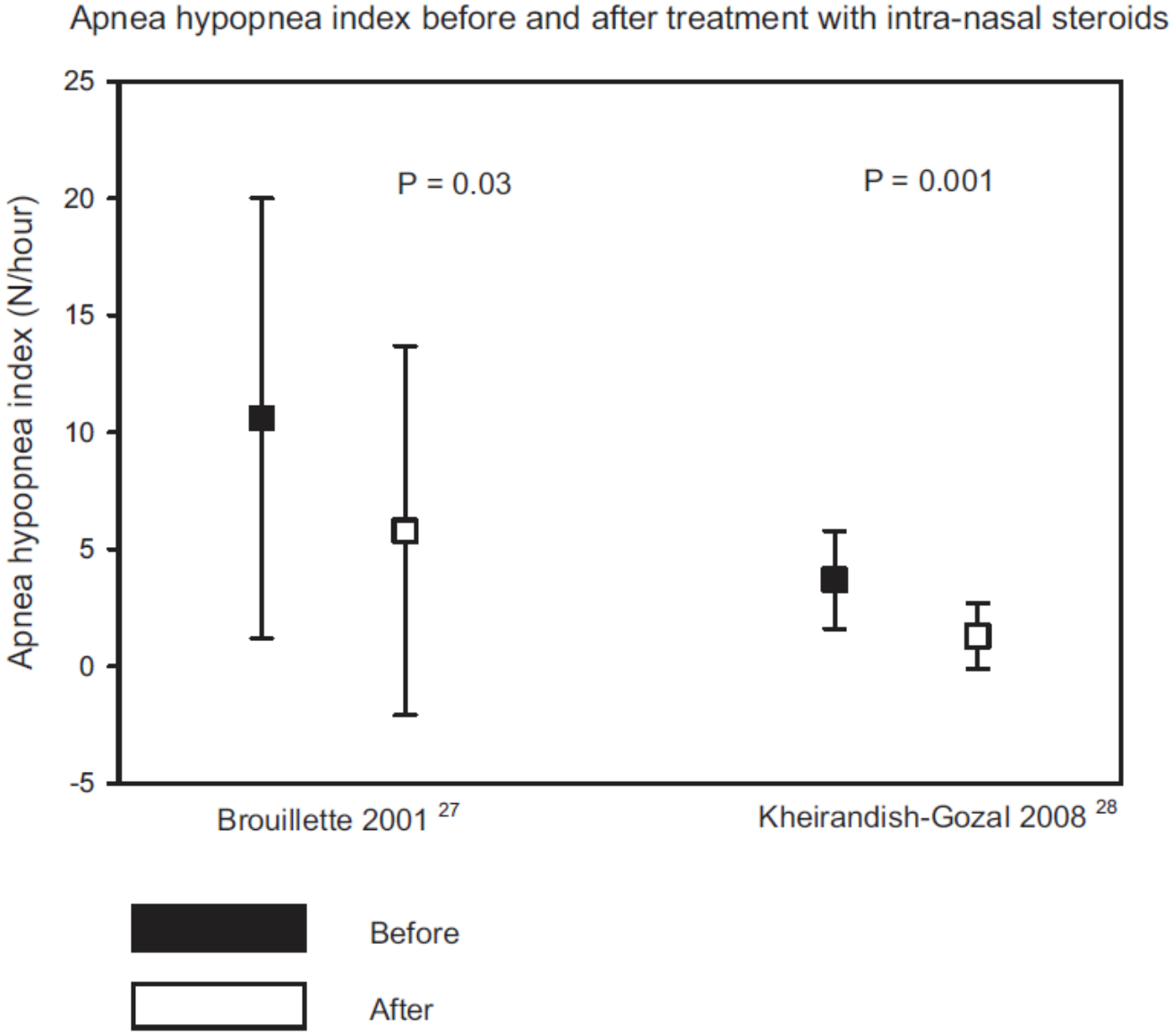


FIGURE 2

Adenoid size (adenoidal/nasopharyngeal ratio) significantly decreased with montelukast. The ratio decreased from 0.81 ± 0.04 before (pre) to 0.57 ± 0.04 after (post) treatment; $P < .001$. In contrast, children who received placebo displayed no significant changes. Star indicates a significant difference between pre and post values.

Goldbart & Tal, Pediatrics 2012


Apnea hypopnea index before and after treatment with intra-nasal steroids
Apnea hypopnea index (N/hour)
25
20
15
10
5
0
-5
P = 0.03
P = 0.001
Brouillette 2001 [27]
Kheirandish-Gozal 2008 [28]
Before
After

Retrospective review – LTA + intranasal CS in mild OSA (AHI <5)

TABLE 2] Changes in Polysomnographic Findings Following 12-Wk Treatment With an Intranasal Corticosteroid and Oral Montelukast in 445 Children

Characteristic	Mild OSA Pretreatment (n = 445)	Mild OSA Posttreament (n = 445)	*P* Value
Age, y	6.2 ± 1.9	6.6 ± 1.9	...
Male sex, %	55.1	...	...
White, %	56.5	...	...
Black, %	26.8	...	...
BMI *z*-score	1.17 ± 0.81	...	...
Obese (BMI *z*-score > 1.65), %	33.8	...	...
Elapsed time between beginning treatment[a] and second NPSG, mean, d	...	114.8 ± 39.2	...
Tonsillar size	2.39 ± 0.77	1.87 ± 0.62	< .01
Adenoid size	2.17 ± 0.77	1.34 ± 0.68	< .001
Mallampati score (n)	1.89 ± 0.62 (412)	1.83 ± 0.64 (412)	...
Total sleep duration, min	472.1 ± 51.2	470.9 ± 49.1	...
Stage 1, %	4.7 ± 3.1	4.2 ± 3.4	...
Stage 2, %	37.8 ± 8.3	29.3 ± 9.7	...
Stage 3, %	40.6 ± 16.2	41.2 ± 15.8	...
REM sleep, %	19.3 ± 6.4	27.5 ± 7.8	< .01
Sleep latency, min	24.7 ± 16.1	27.9 ± 17.2	...
REM latency, min	138.1 ± 54.7	135.3 ± 62.9	...
Total arousal index, events/h TST	15.1 ± 9.3	12.2 ± 8.7	< .01
Respiratory arousal index, events/h TST	2.9 ± 1.7	0.8 ± 1.5	< .001
Obstructive AHI, events/h TST	4.5 ± 2.0 *	1.4 ± 0.0.9	< .01
Spo_2 nadir, %	87.5 ± 3.1	92.3 ± 2.1	< .001
Patients with normal NPSG, No. (%)	...	276 (62.0)	...

Data given as mean ± SD unless otherwise indicated. NPSG = nocturnal polysomnography. See Table 1 legend for expansion of other abbreviations.
[a]Intranasal corticosteroids plus oral montelukast for 12 wk.

LKG, Chest 2014

non-invasive positive pressure ventilation

Main problem – adherence and compliance (4/4)

non-invasive positive pressure ventilation

CPAP - Continuous Positive Airway Pressure (CPAP)

BIPAP – Bi-level positive airway pressure ventilation

APAP - Automatically titrated positive airway pressure

AVAPS - Average volume assured pressure support

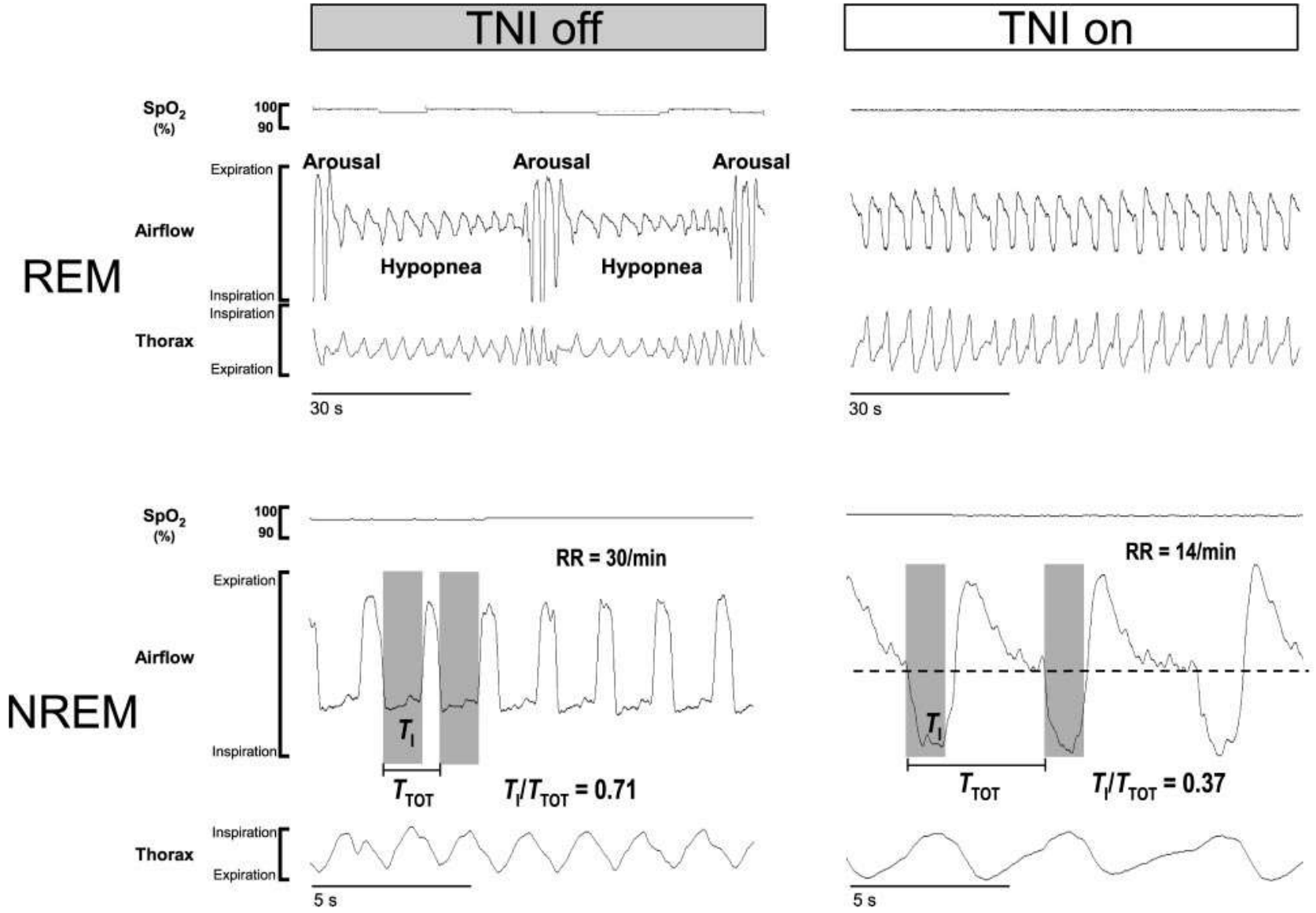
PAV - Proportional assisted ventilation

ASV - Adaptive servo-ventilation

C-Flex®, Bi-Flex® - Expiratory pressure relief and flexible bi-level positive airway pressure

HFHHNC in children

McGinley et al. Pediatrics 2009



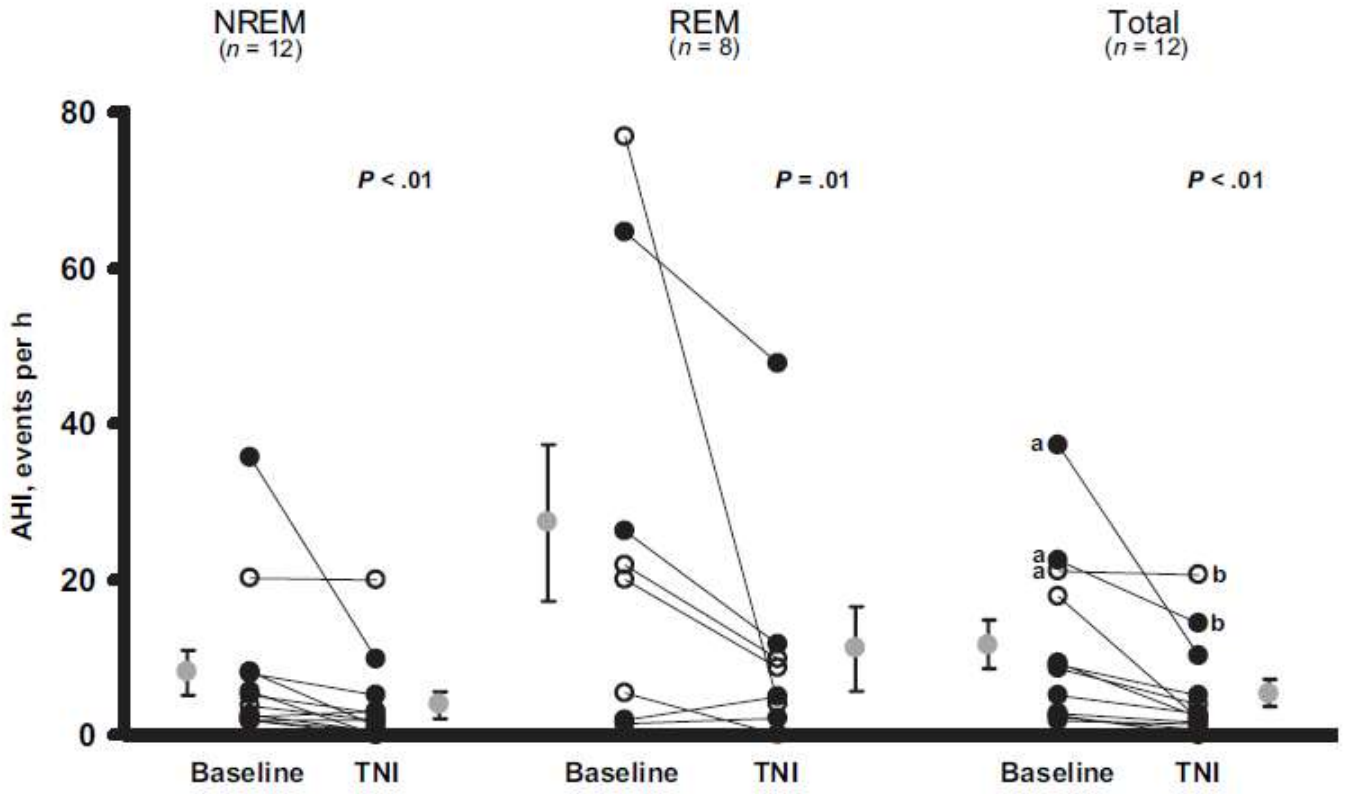
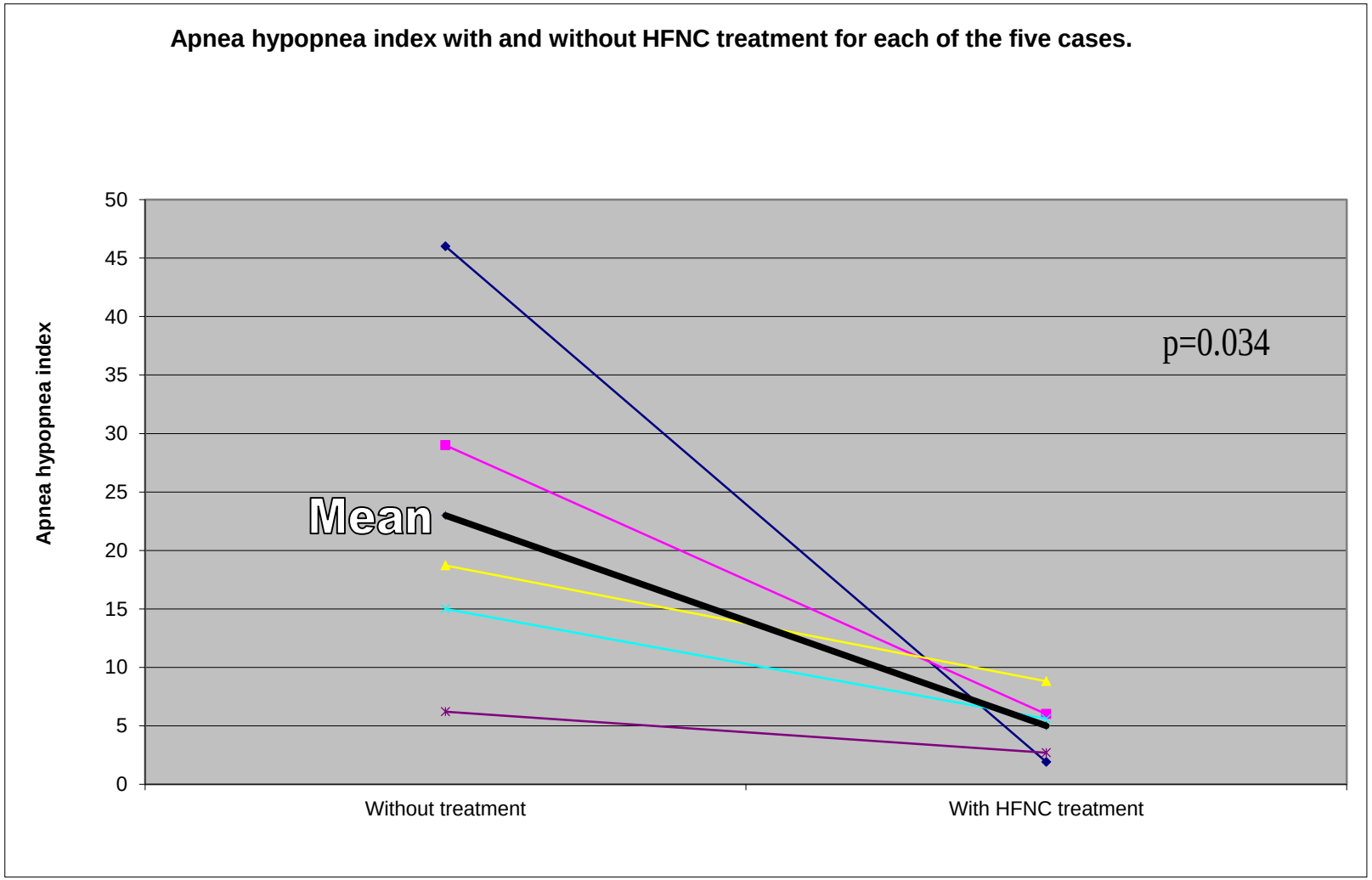


FIGURE 4

The AHIs are displayed for the baseline compared with the TNI-treatment night during NREM (left), REM (middle), and for the entire night (right). Data presented are means ± SEMs. [a] Participants with residual sleep apnea on TNI. [b] Participants with suboptimal AHI responses on TNI compared with CPAP. ○ Children without adenotonsillectomy.

McGinley et al. Pediatrics 2009



Goldberg et Al. 2014


תודה