SLEEP APNEA AND STROKE

Raymond Gottschalk

Overview

- Snoring and sleep apnea (OSA)
- Stroke and OSA/SDB(sleep disordered breathing)
- Evidence of association
- Prevention/therapy
- Summary

Sleep Apnea

- > 18 million affected (1 in 15 in North America)
- Prevalence (Men 24%, Women 9%)
- 10 - 20% are children
- Untreated or undiagnosed >80%
- Health cost for individual with untreated sleep apnea is about $1,336/yr

National Sleep Foundation

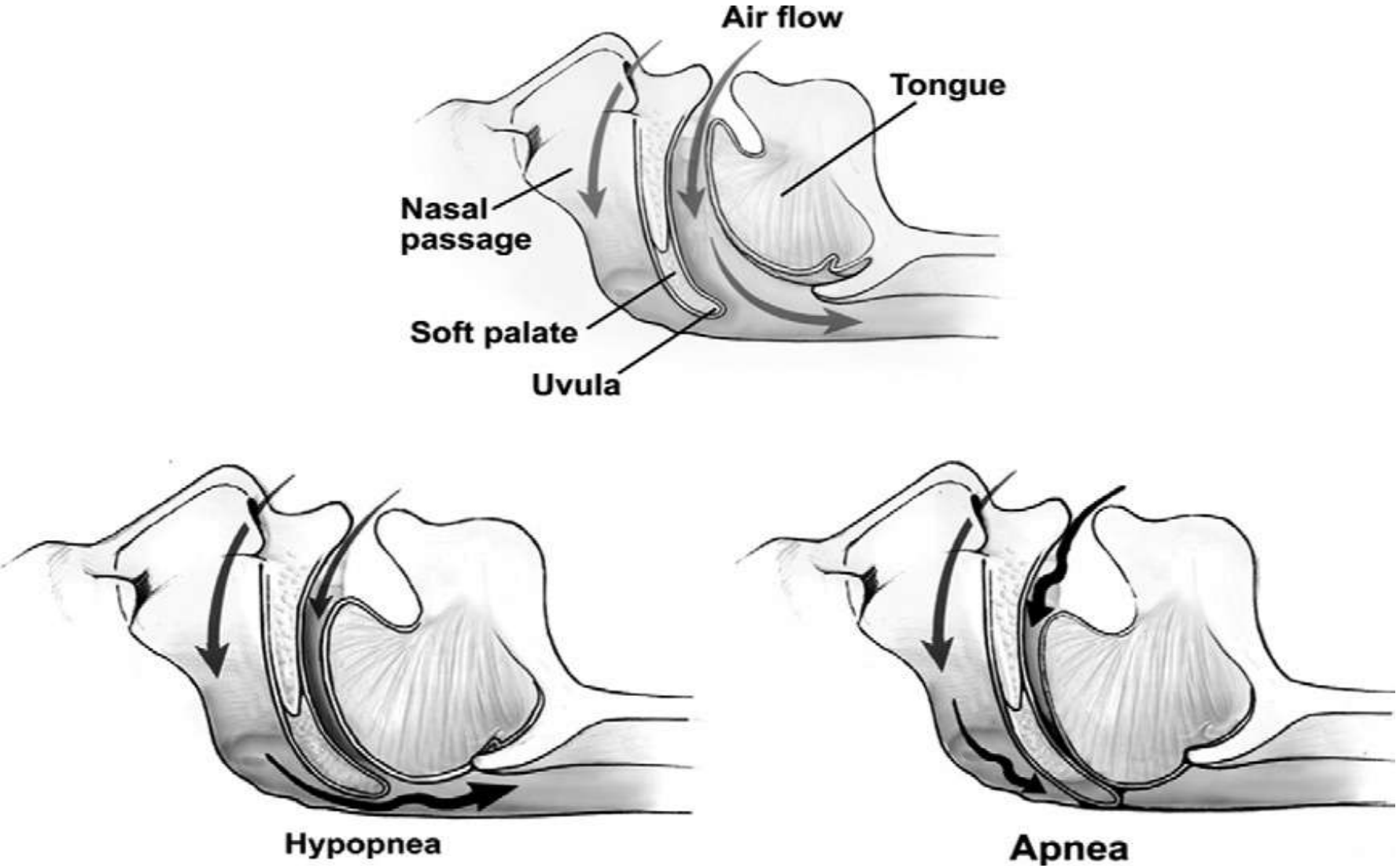
Types of Sleep Apnea

- **Obstructive** (Apnea and Hypopneas, respiratory effort related arousals-RERA)
- Central Sleep Apnea(hypercapnia, eucapnic or hypocapnic)
- Mixed Sleep Apnea

What is Obstructive sleep apnea

- Recurrent episode of airway obstruction during sleep
- lasting at least 10 seconds
- can be associated with arousal or decrease in oxygen level

OSA



Somers et al, JACC

How is OSA measured

AHI (Apnea/hypopnea index) or

RDI (Respiratory Disturbance Index)

- AHI < 5 (normal)
- AHI 5 -15 (mild)
- AHI >15 - 30 (moderate)
- AHI > 30 (severe)
- RERA <10. 10-20 mild, 20-40 moderate and >40 severe

Symptoms/signs of OSA

- Snoring and gasping or choking from sleep
- Excessive daytime sleepiness or fatigue
- Cognitive dysfunction (memory, concentration)
- Change in mood (irritable)
- Unrefreshing sleep
- Waking more tired than when going to bed
- 30% of those with insomnia as presentation have OSA
- Severe cases have cardiac dysfunction and edema

Cause of symptoms

- Hypoxemia (low oxygenation at night)
- Hypercapnia
- Frequent arousal during the night
- Inadequate quality or quantity of sleep
- Cardiac effects
- Brain effects
- Metabolic effects

Untreated OSA increases risk of

- Hypertension
- Heart disease (abnormal rhythm, heart failure)
- **Stroke**
- Depression
- Diabetes
- Accidents
- Death

"Don't step on it . . . it makes you cry."

Stroke

- 2nd - cause of death (worldwide)
- 3rd - cause of death (USA, #1 heart & #2 cancer)
- #1 leading cause of disability in US
- 795,000 cases per annum in US
- 150,000 people die per year
- Stroke health care cost >$40 billion/year

Stroke

- Focal neurologic deficit of vascular origin
- 2-3/1000 per annum
- TIA 20%
- ICHx 15%
- Ischemic stroke 65%

Categories of stroke

- Macrovascular (large vessel)
- Microvascular (small vessel)
- Embolism (usually cardiogenic)
- Other (vasculitis, dissection, coagulability abnormalities)
- Unknown

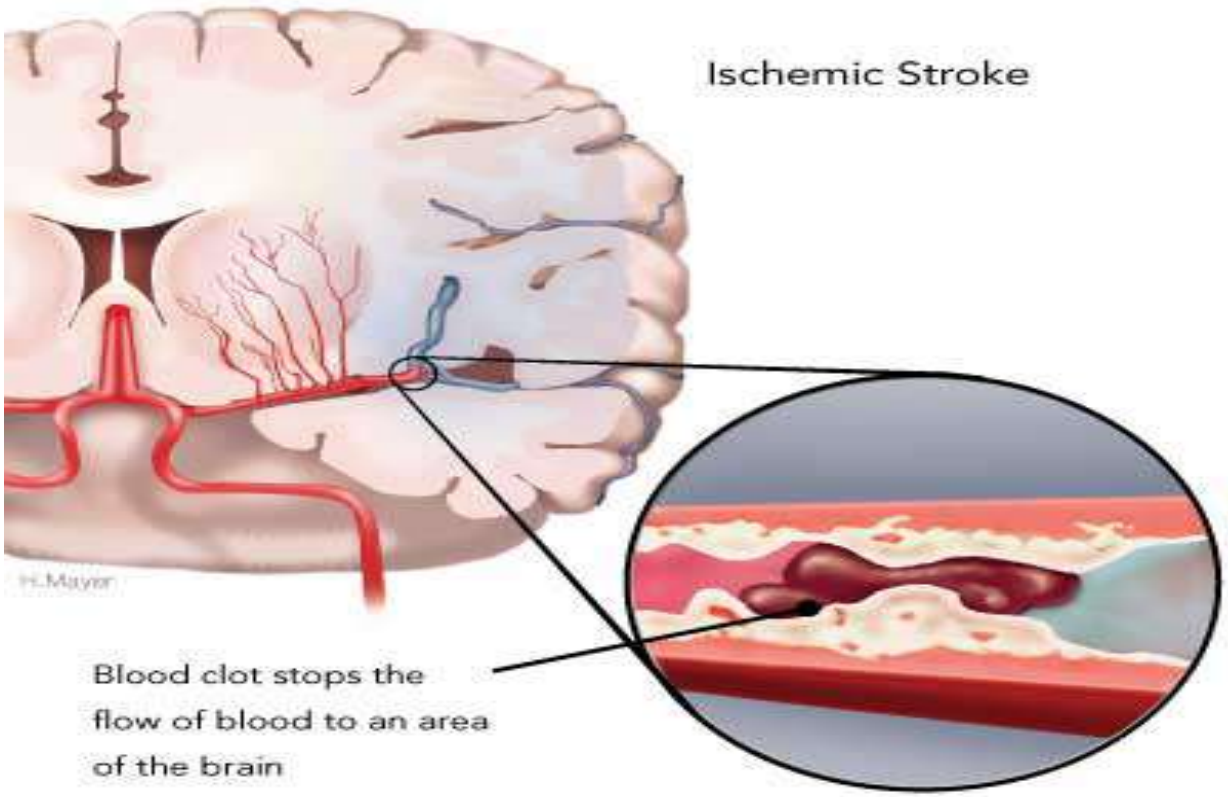
Types of Stroke

- Ischemic stroke (vascular obstruction)

- TIA (transient ischemic attack)- no focal deficit after recovery
    - Mostly seen in OSA patients

- Cerebral Hemorrhage - bleeding into brain and surrounding tissue

Ischemic Stroke



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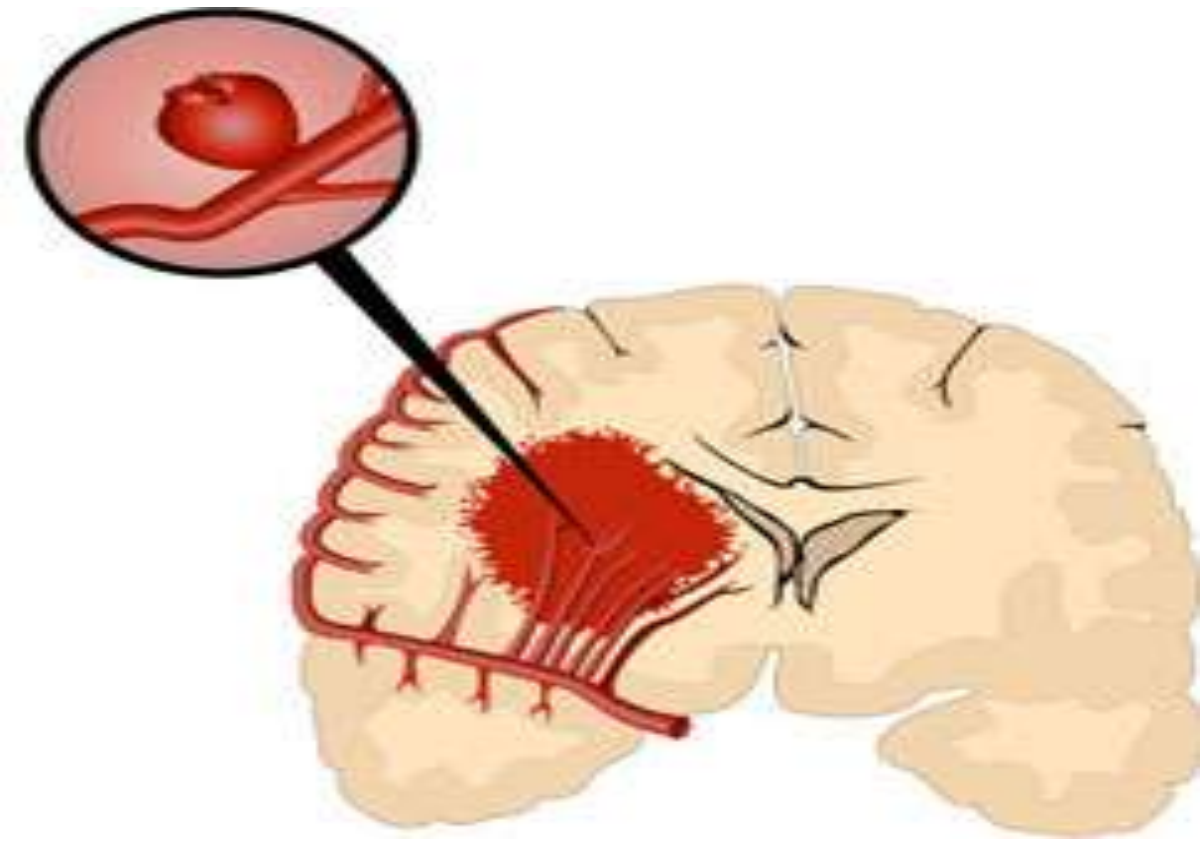
Hemorrhagic stroke



Prevention of stroke is to treat risks

- Hypertension
- Lipids
- BMI
- Atrial fibrillation
- Exercise
- Endarterectomy if 70% stenosis
- Other clotting risks
- Smoking

Risk factors for stroke

- Hypertension
- Heart disease structural and rhythmic
- Diabetes
- High cholesterol
- Smoking
- Age
- **Sleep apnea (OSA)**
- **Obesity**
- **Drugs(cocaine- 1977)**
- John Styth Pemberton –brain tonic 1903)

T.O.
COSTA COKEFORDIA

History of stroke and breathing

- John Cheyne 1818 – periodic breathing and apoplexy
- CSR with bilateral stroke
- Broadbent 1877 - OSA with ICHx
- Ratto 1955- Ondine's curse with brainstem stroke

Stroke

- OSA is common in Stroke (70%)
- Stroke occurs in early morning (4am and 12 pm)
- Increase risk with higher AHI/RDI
- Increase risk with age
- Increase risk in people who have sleep apnea and heart disease
- OSA worsens after stroke (esp acute phase)

SDB and stroke studies to review

- Yaggi (2004) – 1022 subjects for 6 years
  - If AHI >36 had hazard ratio of 3.3
- Marin (2005) – 1387 males for 10 years snorers vs control
  - If AHI >30 risk was increased vs mild OSA
- Arzt (2005) – 1475 subjects AHI >20 had OR of 4.3
- Munoz (2005) – elderly >70 years AHI>30 had HR 0f 2.5
- Minoguchi (2007) – silent stroke or white matter disease on MRI if AHI>30

Study from Yaggi et al

- Conducted at Yale Medical Center
- 1022 participants enrolled but only 842 completed
  - 573 with OSA (AHI- 35), 325 w/o OSA (AHI<2)
- Mean age - 60yrs old
- Follow up of 2-4yrs
- Adjusted for age/sex/race, smoking, alcohol intake, BMI, DM, HTN, AF, high cholesterol.

Results

- OSA group - 22 stroke, 50 death
- Control group - 2 stroke, 16 death

Hazard ratio 1.97; (95% CI 1.12-3.48), P=0.01

Yaggi et al, NEJM, 2005

More evidence

- Another study of 1189 subjects from the general population
- Individuals (#99) with Sleep apnea (AHI>20) was associated with increased risk of having a stroke

(OR 4.31; 95% CI 1.31-14.15; P=0.02)

Arzt et al, AM J Respir Crit care Med, 2005

Stroke and SDB

- Johnson KG (2010)- meta-analysis of stroke or TIA found AHI>5 in 72%
- AHI>20 was 38%
- Only 7% of SDB was central
- Recurrent stroke had higher level of SDB
- About 50% of subjects with stroke have AHI>10

What connects OSA to stroke

- **Sleep apnea increase risk of:**

Hypertension
Heart disease
Arrhythmia
Diabetes

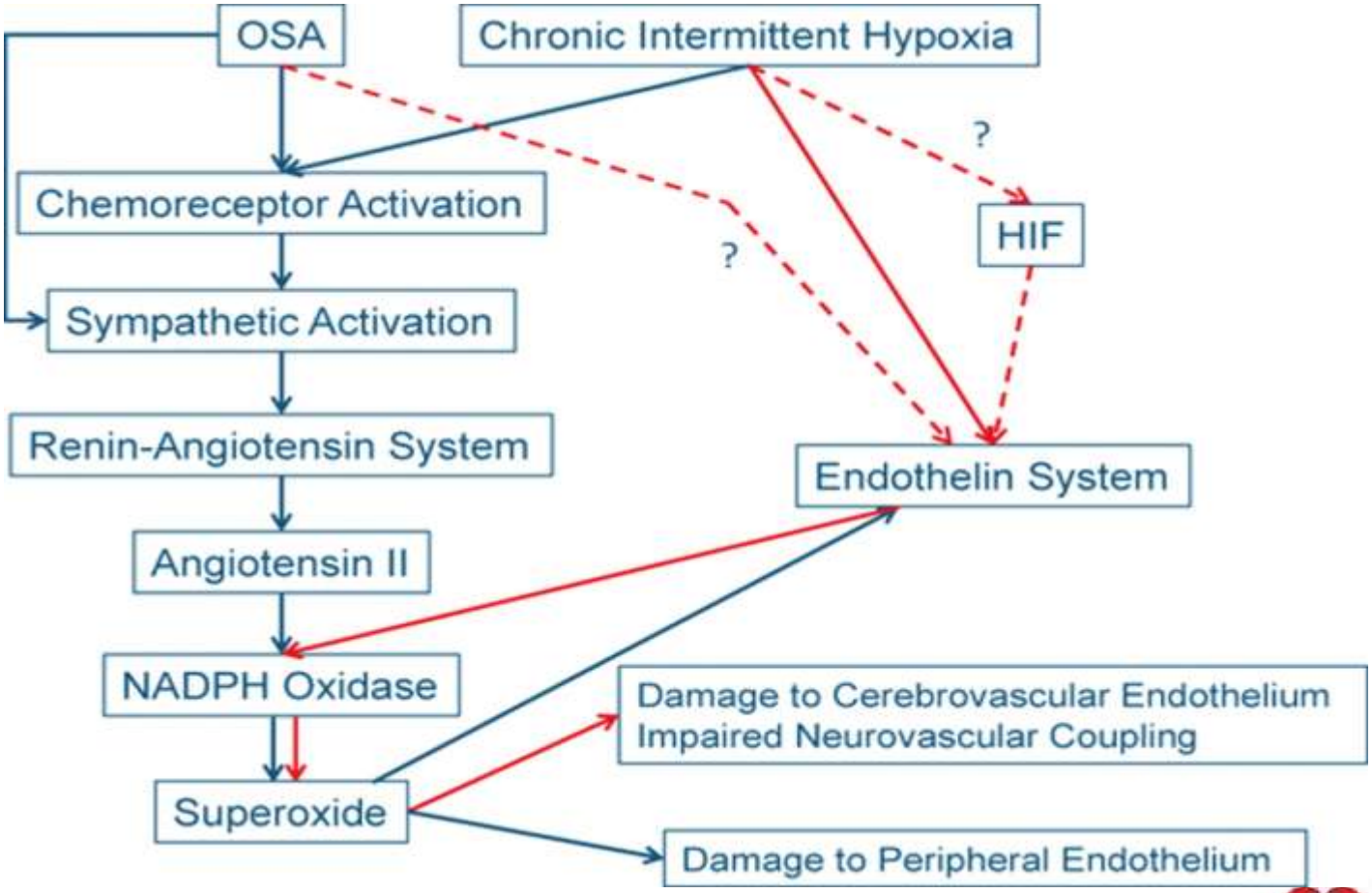
- **Stroke risk factors are**

Hypertension
Heart disease
Atrial fibrillation
Diabetes

How does sleep apnea lead to stroke

- Decrease cerebral blood flow during apnea
- Hypoxemia **(low oxygenation)**
- Sympathetic activation **(increase BP/HR)**
- **Abnormal heart rhythm and rate**

Proposed pathway for activation of NADPH oxidase, generation of superoxide, and upregulation of the endothelin system in the peripheral circulation after OSA and chronic intermittent hypoxia (black lines).



Durgan D J , and Bryan R M J Am Heart Assoc 2012;1:e000091

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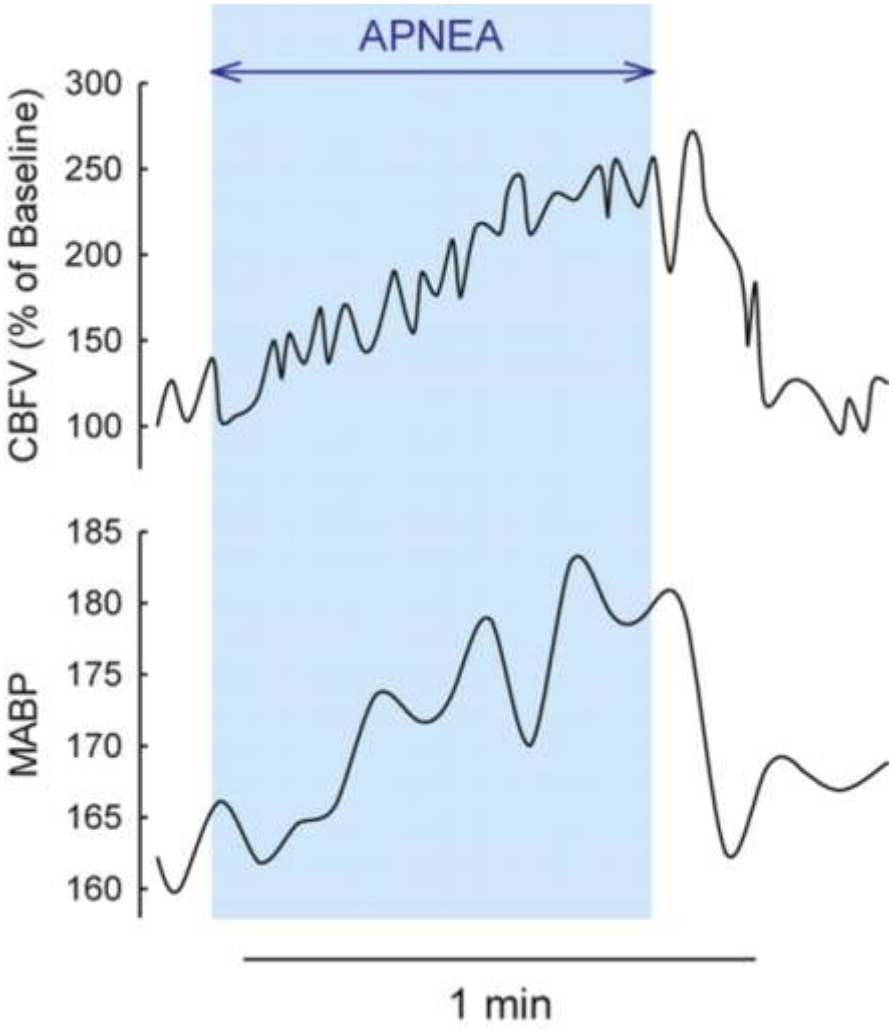
Changes in blood flow velocity in the middle cerebral artery (CBFV; top) and mean arterial blood pressure (MABP; bottom) during an episode of apnea (shaded in light blue).



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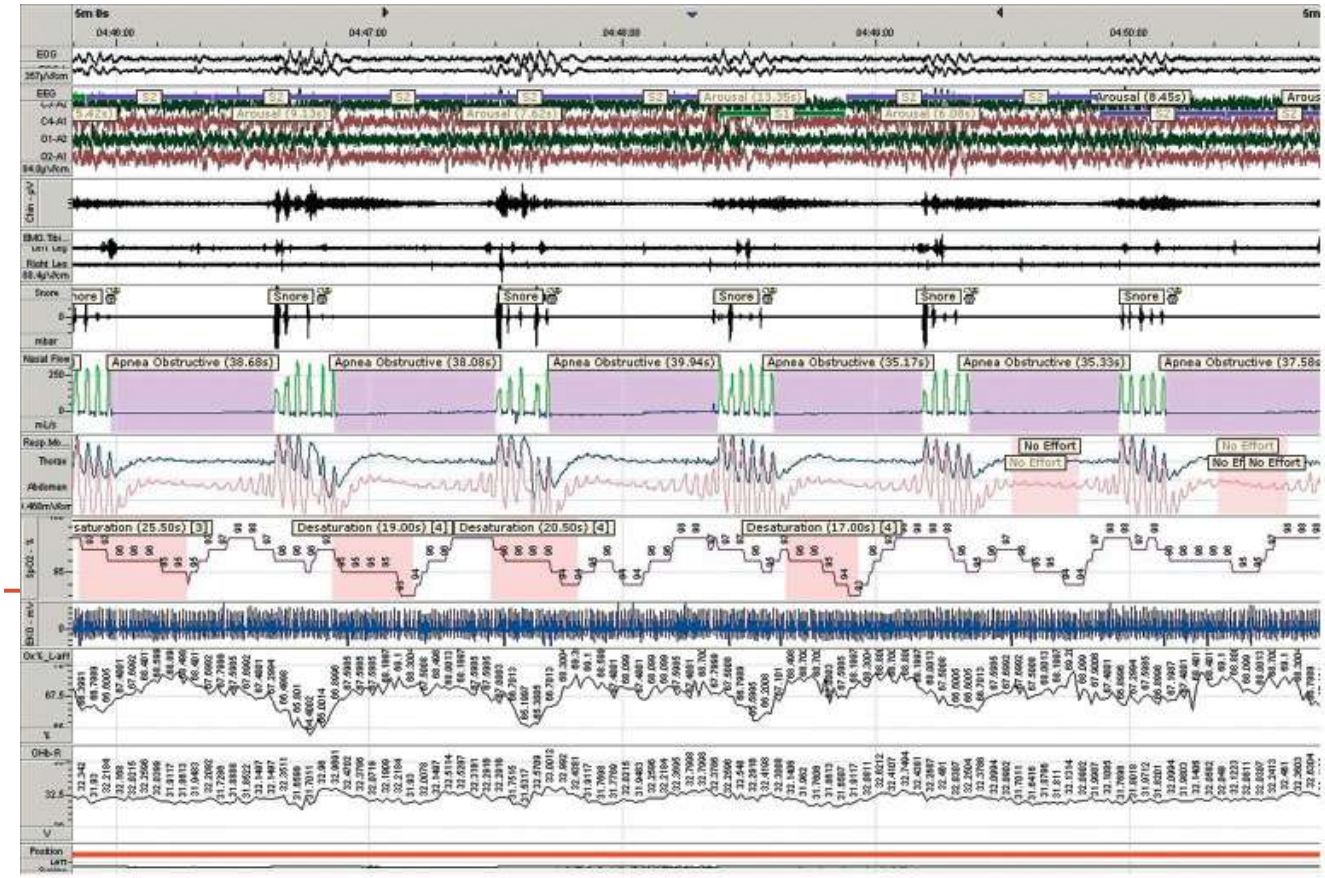
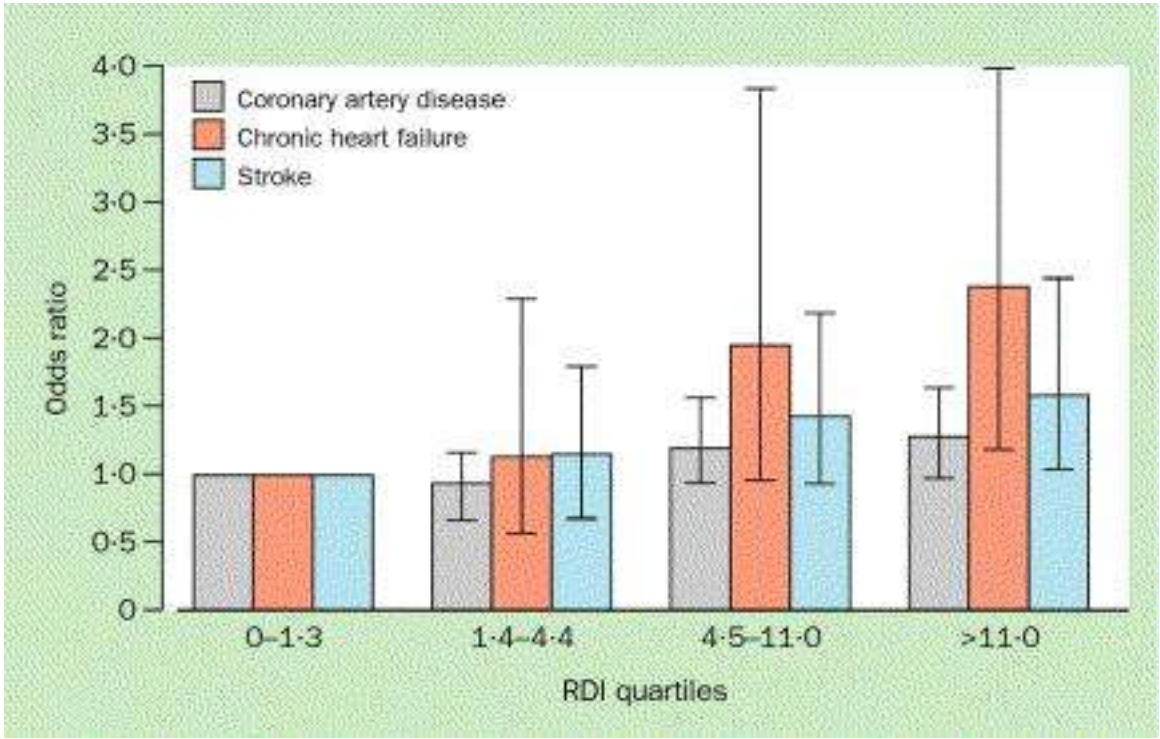


Figure 88-1 Obstructive sleep apnea in acute ischemic stroke. This 70-year-old man (HRS) has left middle cerebral artery stroke, carotid artery occlusion, and atrial fibrillation. He has habitual snoring but no excessive daytime sleepiness on history. Aphasia and severe hemiparesis are clinically apparent. National Institutes of Health (NIH) stroke score is16, and there are no signs of heart failure. Polysomnography 2 days after stroke onset shows an apnea–hypopnea index (AHI) of 79 (33 obstructive, 42 mixed) and minimal oxygen desaturation of 85%. The AHI is normalized (<5/hr) with continuous positive airway pressure (CPAP).

(MRI pictures courtesy of Prof. A. Valavanis, Institute of Neuroradiology, University Hospital, Zürich, Switzerland.)

Increase in vascular disease with increase in RDI



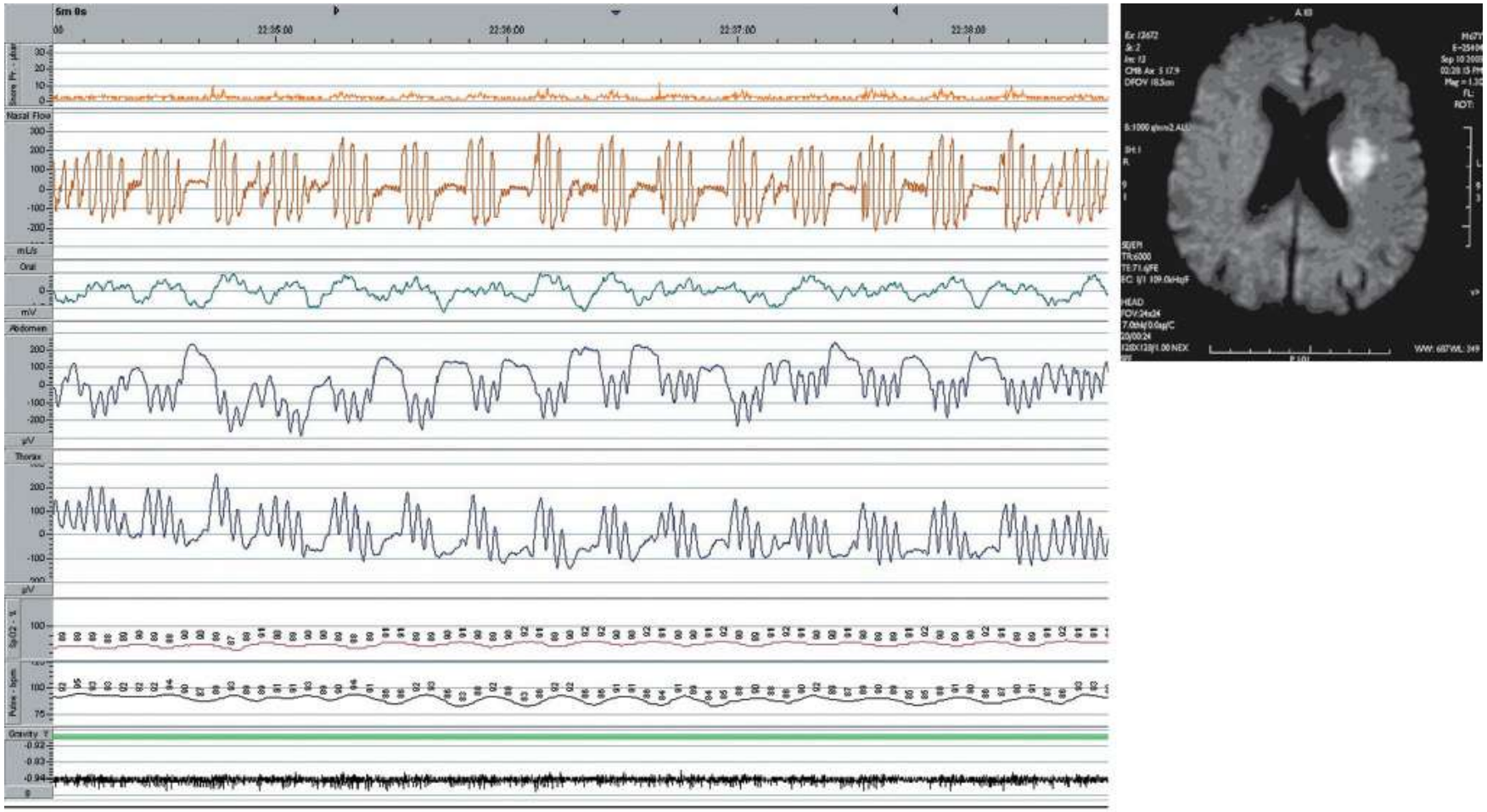


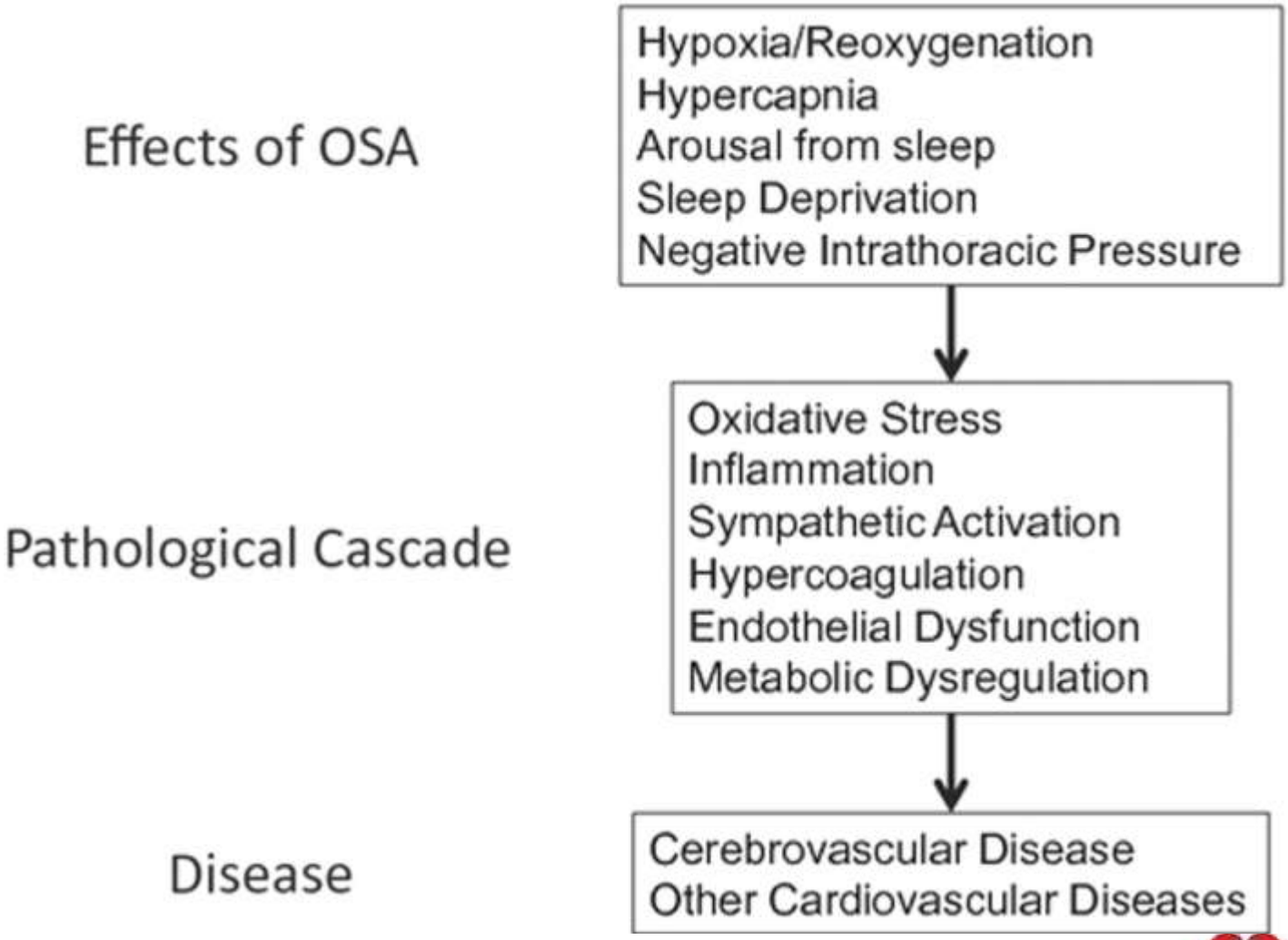
Figure 88-2 Central sleep apnea in acute ischemic stroke. This 63-year-old man (PD) had a left subcortical stroke of unknown origin, with arterial hypertension and habitual snoring but no excessive daytime sleepiness on history. He had clinically mild hemiparesis, with a National Institutes of Health (NIH) Stroke Score of 8 and no signs of heart failure (cardiac ejection fraction, 55%). Polysomnography the first night after stroke onset showed an apnea–hypopnea index (AHI) of 53 (mainly central). The patient spontaneously improved after 1 week (AHI, 16).

(MRI pictures courtesy of Prof. G. Schroth, Institute of Neuroradiology, University Hospital, Bern, Switzerland.)

How does sleep apnea lead to stroke

- Coagulation **(increase blood clot formation)**
- Disruption of lining of blood vessels
- Inflammatory markers (CRP, IL6)
- Metabolic deregulation (Insulin, leptin)

The effects of OSA lead to a pathological cascade that is responsible for cerebrovascular and other cardiovascular diseases.



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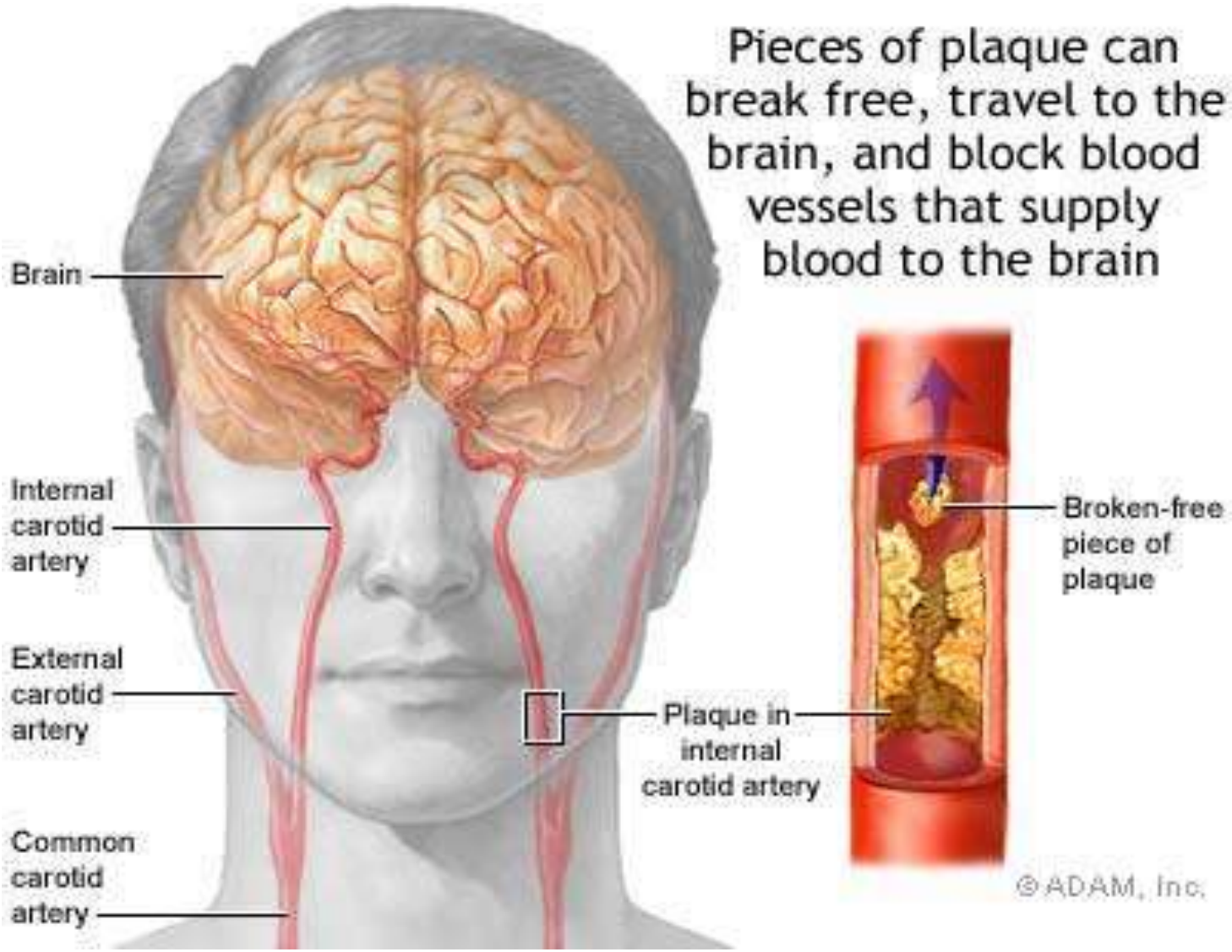
Snoring

- Studies suggest it is a risk factor for ischemic stroke
- Multiple Studies show it increases blood pressure
- Vibration from snoring increase plaque formation in the carotid artery.


Pieces of plaque can break free, travel to the brain, and block blood vessels that supply blood to the brain
Brain
Internal carotid artery
External carotid artery
Common carotid artery
Plaque in internal carotid artery
Broken-free piece of plaque
© ADAM, Inc.

Snoring

- Study from Japan
- 167 patients with OSA
- mean age - 47
- After control for High BP, DM, high cholesterol
- Results shows patients with
  - High AHI have increase carotid artery thickness (measured by ultrasound)
  - Decrease thickness after CPAP therapy

Suzuki et al, Sleep, 2004

Brain scan in OSA patients

- Brain MRI shows silent brain infarct in 25% of patient with moderate to severe OSA

Minoguchi et al, AM J Respir Crit care Med, 2007

- Higher prevalence of sleep apnea in patients with vascular dementia compared with patients with Alzheimer's disease or control of similar age

Erkinjuntti et al, sleep, 1987

How does the Presence of OSA Affect Stroke Recovery?

- Studies suggest that stroke patients with OSA have
  - Reduce motivation
  - decrease cognitive capacity
  - Prolong rehab stay
  - May increase the risk of recurrent stroke and death.
  - ??Conditioning effect of mild hypoxemia??

Sleep apnea treatment

- Weight loss
- Sleep with head elevated with wedge or pillow
- Avoid sleeping supine
- Avoid alcohol consumption at night
- Stopping smoking
- Improving nasal patency
- Upper airway surgery
- PAP devices
- Bypassing the airway

Effect of PAP therapy

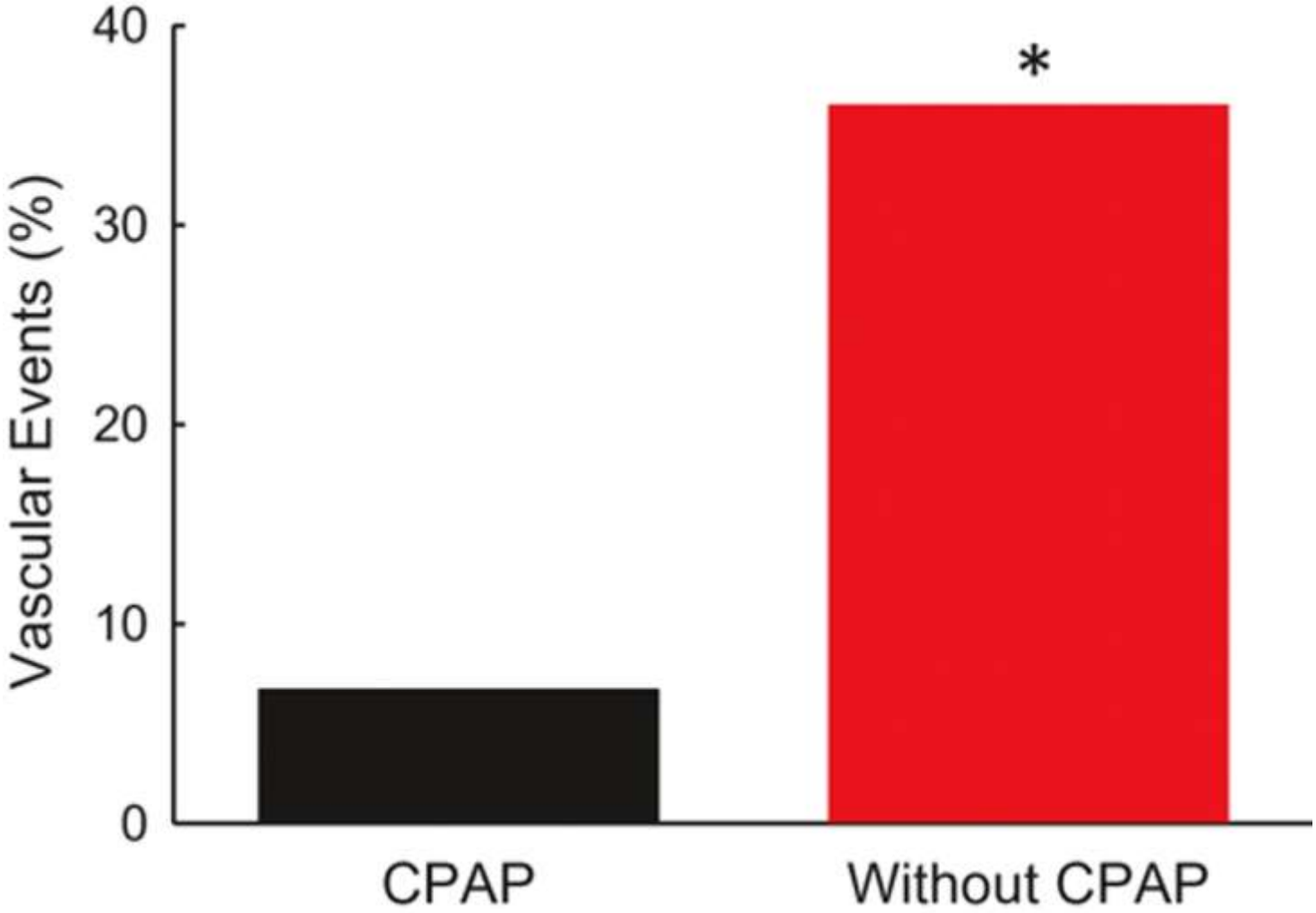
CPAP

BiPAP

ASV

Other forms of ventilation

Incidence of vascular events over an 18-month period after stroke in CPAP users (n=15) and those who discontinued the use of CPAP (n=36).



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Use of CPAP and stroke risk

- Successful treatment of sleep apnea with CPAP lowers blood pressure.

  (indirectly lowers the risk of stroke)
- Improves blood flow to the brain
- CPAP therapy reduces mortality, especially after stroke.

CPAP Study

- 5yr follow study from Spain
- 166 patients with stroke
- CPAP treatment offered to patient with AHI > 20
- Patient followed for 1,3,6, then q6 months for 5 yrs

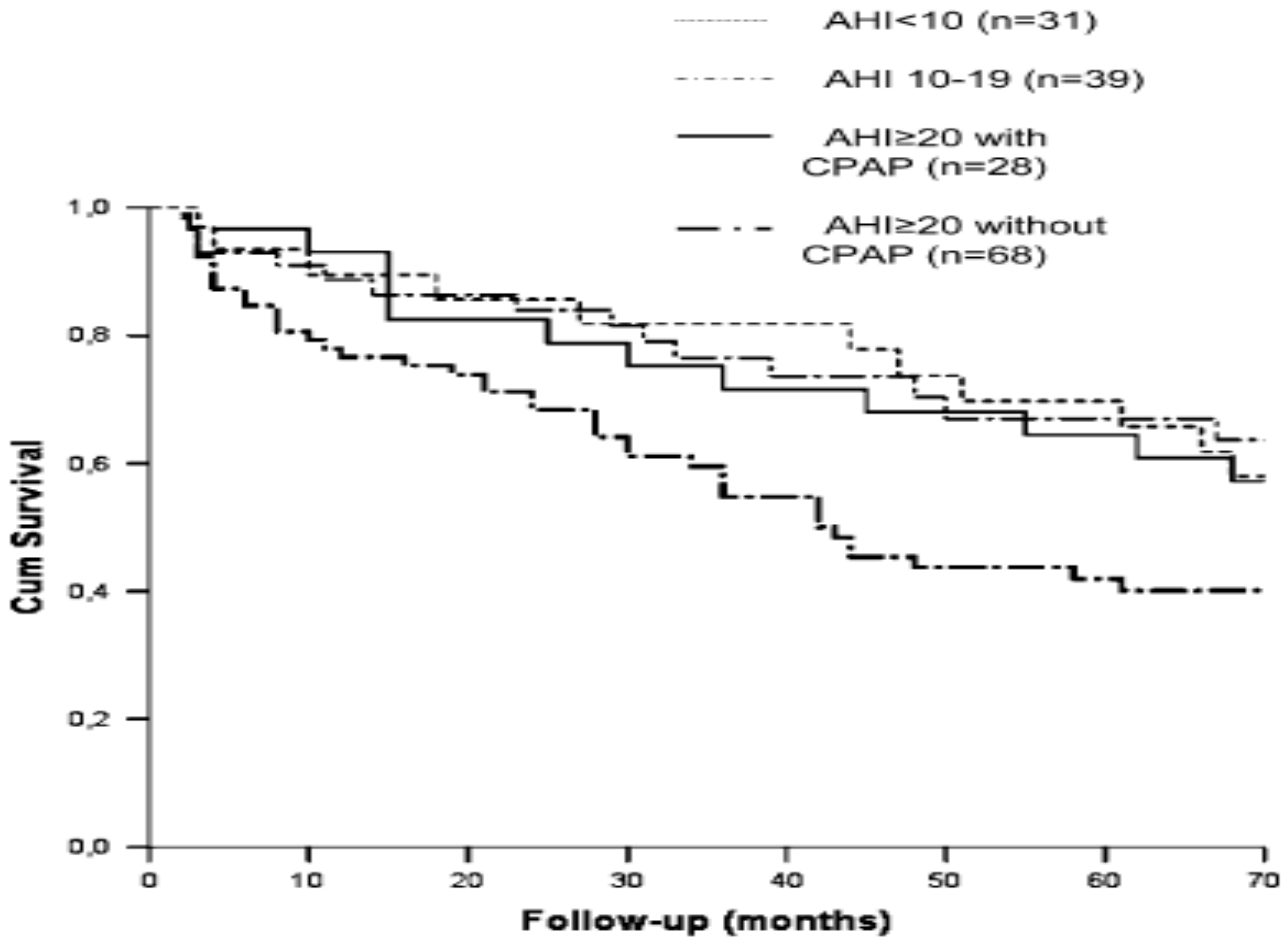

Figure 2. Accumulated survival curve for study groups of patients with stroke, by apnea–hypopnea index (AHI) cutoff point and continuous airway pressure (CPAP) tolerance. The group of patients with stroke with an AHI of 20 or greater and poor tolerance of CPAP showed more mortality than the rest of the patients after 5 years of follow-up. Cum = cumulative.

Martinez-garcia et al, Am J respir Crit Care med, 2009

Issues of CPAP adherence

- Study of 105 pts shows only about <70% of patient with OSA and stroke actually adhere to CPAP therapy
- CPAP compliance is poor
- Difficulty using mask
- Motor deficit (facial weakness)
- Difficulty understanding
- Difficulty applying mask

Wessendorf et al

Other OSA treatments

- But no studies to justify efficacy
  - Oral appliances(may decrease snoring)
  - Surgery (Jaw advancement, soft tissue)

Cure for OSA

- Tracheotomy

Summary

- OSA is a risk factor for Stroke
- OSA increases risk of stroke and death
- OSA needs to be treated
- Evidence shows CPAP decreases the risk of stroke and mortality in OSA patients

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