ΑΝΑΠΝΕΥΣΤΙΚΕΣ ΔΙΑΤΑΡΑΧΕΣ ΣΤΟΝ ΥΠΝΟ ΣΕ ΑΣΘΕΝΕῖΣ ΜΕ ΑΝΟΙΑ

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Leading Causes of Death in Perspective

- war
- pregnancy & birth
- medical complications
- murder
- undetermined events
- mental health disorders
- transport accidents
- suicide
- musculoskeletal disorders
- diabetes
- non-transport accidents
- infections
- kidney disorders
- digestive disorders
- nervous system disorders

Alzheimer’s Disease
<table>
<thead>
<tr>
<th>Rank</th>
<th>Disease Description</th>
<th>Male Cases</th>
<th>Female Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Coronary heart disease (I20–I25)</td>
<td>11,016</td>
<td>8,750</td>
</tr>
<tr>
<td>2</td>
<td>Dementia and Alzheimer disease (F01, F03, G30)</td>
<td>3,656</td>
<td>7,277</td>
</tr>
<tr>
<td>3</td>
<td>Cerebrovascular disease (I60–I69)</td>
<td>4,181</td>
<td>6,368</td>
</tr>
<tr>
<td>4</td>
<td>Lung cancer (C33, C34)</td>
<td>4,995</td>
<td>3,222</td>
</tr>
<tr>
<td>5</td>
<td>Chronic obstructive pulmonary disease (COPD) (J40–J44)</td>
<td>3,572</td>
<td>2,890</td>
</tr>
</tbody>
</table>
Clinical Progression of AD and MCI

- **MCI**
  - MMSE 24–30
  - Mild subjective/objective memory loss
  - Normal function

- **Mild AD**
  - MMSE 20–23
  - Forgetfulness
  - Repetitive questions
  - Daily function impaired

- **Moderate AD**
  - MMSE 10–19
  - Progression of cognitive deficits
  - Short-term memory loss
  - Word-finding difficulties

- **Severe AD**
  - MMSE 0–9
  - Agitation
  - Altered sleep patterns
  - Total dependence: dressing, feeding, bathing

Vanderbilt University Medical Center
Department of Neurology
Prevalent sleep problems in the aged.

Ancoli-Israel S¹, Kripke DF.

Abstract

Quality of sleep influences the level of daytime functioning, including stress levels, psychosomatic complaints, general health, and overall well-being. As people age, they complain more about disturbed sleep, insomnia, increased time in bed, and sleep fragmentation. These complaints can be related to circadian rhythm desynchronization, hypnotic or other medication use, chronic bedrest, napping, dementia, or to sleep apnea, a disorder of respiratory cessation which is quite prevalent in the elderly. We review here the results of 12 years of research on sleep in the elderly. In studies of three populations of elderly, it was found that between 24% and 42% had five or more apneas per hour of sleep and 4%-14% had 20 or more apneas per hour of sleep. Since apnea is related to dementia and even to mortality, this high prevalence of apnea is of extreme importance.
Sleep-disordered Breathing

• Other Symptoms
  – Snoring
  – Restless sleep
  – Choking/gasping during sleep
  – Witnessed apnea
Sleep-disordered Breathing

• Significance, Signs, and Symptoms
  ◦ Daytime somnolence, effect on function
  ◦ **Decreased cognition, dementia may be worse**
  ◦ CHF, arrhythmias, HTN, cor-pulmonale
  ◦ Polycythemia
  ◦ Nocturia
  ◦ **Personality changes**
  ◦ Morning headaches
  ◦ Decreased libido, impotence
  ◦ May increase mortality
Prevalence of Sleep Disturbances in Mild Cognitive Impairment and Dementing Disorders: A Multicenter Italian Clinical Cross-Sectional Study on 431 Patients
Prevalence of Sleep Disturbances in Mild Cognitive Impairment and Dementing Disorders: A Multicenter Italian Clinical Cross-Sectional Study on 431 Patients
PSQI. In this population, almost 60% had symptoms clinically compatible with SDB and more than 50% had EDS and insomnia. The frequency of sleep disturbances found in this study is in line with the results of previous studies. The score of depressive symptoms was more severe in persons presenting any of the investigated sleep disorders. Depressive symptoms are common in older adults, risk increase with respect to AD was for SBD and this result is in agreement with the high frequency of obstructive sleep apneas reported in patients with stroke [15].
Association of sleep-disordered breathing with decreased cognitive function among patients with dementia

KIYOAKI AOKI¹,², MASAHIRO MATSUO¹, MASAHIRO TAKAHASHI¹, JUNICHI MURAKAMI³, YASUSUKE AOKI², NAOSUKE AOKI², HIROTAKA MIZUMOTO², AYAKO NAMIKAWA², HIROKO HARA², MASAHARU MIYAGAWA⁴, HIROSHI KADOTANI¹ and NAOTO YAMADA¹

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**Figure 1.** Prevalence and severity of dementia in each sleep-disordered breathing (SDB) condition.

**Figure 2.** Prevalence and severity of dementia in each sleep-disordered breathing (SDB) condition.
Association of sleep-disordered breathing with decreased cognitive function among patients with dementia

KIYOAKI AOKI¹·², MASAKI KUROSE³, MASAKI TAKAHASHI¹, JUNICHI MURAKAMI¹, YASUSUKE AOKI¹, NAOSUKE AOKI¹, HIROTAKA MIZUMOTO², AYAKO NAMIKAWA², HIROKO HARA², MASAHARU MIYAGAWA³, HIROSHI KADOTANI¹ and NAOTO YAMADA¹

(a) Age <80 years old

(b) Age ≥80 years old
Prevalent sleep problems in the aged.

Ancoli-Israel S¹, Kripke DF.

Abstract
Quality of sleep was studied in the elderly. The complaints manifest variously, from disturbed sleep, insomnia, and nightmares, to disturbances of the circadian rhythm. Related to circadian rhythm disturbances are disturbances of daytime activity. We reviewed here the results of 12 years of research on the prevalence of respiratory disturbances in three populations of elderly. It was found that between 24% and 42% had apnea during their sleep, and 4%-14% had 20 or more apneas per hour of sleep. Since sleep apnea is definitely related to dementia and even to mortality, this high prevalence of apnea is of extreme importance.

20-40% AHI=5/ώρα
4-14% AHI>20/ώρα

ΑΠΟΤΕΛΕΣΜΑ: άνοια και θησαυρότητα!

Οι ηλικιωμένοι...
Anatomic and physiopathologic changes affecting the airway of the elderly patient: implications for geriatric-focused airway management

Kathleen N Johnson Daniel B Botros Leanne Groban Yvon F Bryan
The physical history ...
OBSTRUCTIVE SLEEP APNEA

NASAL/ORAL AIRFLOW

THORACIC RESPIRATION

O₂ SATURATION

100%
50%
0%

10 SECONDS
Sleep apnea syndrome of moderate to severe intensity affects
  – 17% of 50-70 year-old men
  – 9% of 50-70 year-old women

Peppard PE et al. Am J Epidemiol 2013
Sleep apnea and dementia
Arousal response is associated with:

- Sympathetic surges
  - at termination of sleep apnea events
  - more active in REM sleep
  - decline in SWS
FACTORS CONTRIBUTING TO CEREBROVASCULAR DISEASE IN SLEEP APNEA

- Increased sympathetic drive and tone
- Surges in blood pressure
- Atrial fibrillation
- Patent foramen ovale
- Hemodynamic changes
- Autoregulation
- Hypoxia
- Systemic inflammation
- Endothelial dysfunction
- Hypercapnia
- Hypercoagulability
– Cerebral hemodynamic autoregulatory mechanisms fail (measured using cerebral infrared spectroscopy) with brain hypoxia in the presence of frequent apneas (AHI > 30) and obstructive events

Pizza F et al. Sleep. 2010;33:205
Repeated hypoxia may damage the endothelium and trigger the release of pro-inflammatory factors

- plasma cytokines
- tumor necrosis factor-alpha
- interleukin-6

HYPOXIA

• Hypoxia and inflammation are intertwined at the molecular, cellular, and clinical levels

• OSA >15 AHI is a risk factor for cerebral white matter changes in middle-aged and older patients
  – OR: 2.08 [95% (CI): 1.05-4.13]

Kim H et al. Sleep 2013;36:709
• OSA is a risk factor for subcortical ischemic vascular dementia

Fig 4.—Coronal section of cerebral hemispheres shows similar anatomic configuration of arteries for deep
Sleep wakefulness, EEG delta power, and body temperature (IH+SF).

Intermittent hypoxia + sleep fragmentation

A. WT
B. hApoE4
C. % time wake
D. % time SWS
E. % time REM
F. % time REM
G. Wake episodes
H. Wake episodes
I. Body temperature °C
J. Body temperature °C

Navita Kaushal et al. Am J Physiol Regul Integr Comp Physiol 2012;303:R19-R29

©2012 by American Physiological Society
Data shown are mean NREM sleep latency values (seconds) obtained using murine multiple sleep latency test.
pathophysiology
4. The hippocampus is found to be significantly smaller in people with obstructive sleep apnea. This area of the brain processes short and long-term memory and spatial navigation. One study found that hippocampal

5. Mammary bodies are important for memory recall, as well as for memory for certain smells. These structures are much smaller in patients
From: Changes in cerebral metabolites in obstructive sleep apnea: a systemic review and meta-analysis

Neuropsychological deficits in OSA

- Fine motor coordination ↓
- Executive function ↓
- Attention/Vigilance ↓
- Memory, learning ↓

Frontal lobe: NAA/Cho ↓

Temporal lobe: NAA ↓, Cho/Cr ↑, ml/Cr ↑

Thalamus: Cho/Cr ↑

Occipital lobe: ml ↑

Insula: NAA/Cr ↓, ml/Cr ↑, ml/NAA ↓, Glx ↑

Hippocampus: NAA/Cr ↓, Cho/Cr ↓
Sleep apnea, apolipoprotein epsilon 4 allele, and TBI: Mechanism for cognitive dysfunction and development of dementia

Ruth O’Hara, PhD,1,2 Avinoam Luzon, BS,2 Jeffrey Hubbard, BA,1,2 Jamie M. Zeltzer, PhD1,2

**Figure 1.**
Mediator model: Proposed model for obstructive sleep apnea (OSA) mediating negative association of apolipoprotein epsilon 4 (APOE ε4) on cognitive function in traumatic brain injury (TBI) patients. In this model, a significant association is found between APOE ε4 allele and OSA and OSA is responsible for observed increase in cognitive impairment and dementia in those with APOE ε4 allele; those without APOE ε4 allele display decreased OSA and no increase in cognitive impairment and dementia.
OSA Treatment

• Weight loss, avoid supine position (tennis balls)
• Avoid sedating drugs
• Prescription drugs not helpful
• CPAP/BIPAP – Most efficacious
  ◦ Compliance issues
• Oral appliance – less effective, use for mild cases or if CPAP not tolerated
• Surgery – trach, uvuloplasty, bariatric surgery – not first line, various effectiveness
Conclusions

Donepezil treatment improved AHI and oxygen saturation in patients with Alzheimer disease. Treatment also increased REM sleep duration and reduced ADAS-cog scores.

Trial registration

ClinicalTrials.gov Identifier: NCT00480870.
CPAP and COGNITIVE IMPAIRMENT

• In a study of patients with minimal cognitive impairment or with Alzheimer disease, patients with sleep apnea started cognitive decline at an earlier age
  – (MC1: 72.63 vs 83.67; MC2: 72.15 vs 83.45; MC3: 77.40 vs 89.89; p < 0.01).
  – (AC3: 83.46 vs 88.13; p < 0.05)

• Treatment with CPAP delayed initiation or slowed progression of cognitive changes
  – CMC1: 72.63 vs 82.10; CMC2: 72.11 vs 82.10; p < 0.01).

Osorio RS et al. Neurology. 2015.12;84:1964
Comorbid Alzheimer’s Disease and OSAS: Does CPAP Slow Cognitive Decline?

OSAS is common in patients with AD, with a greater than 40% prevalence in those who are institutionalized. Unfortunately, few behavior or pharmacologic interventions effectively delay cognitive decline and preserve nighttime sleep duration and quality in older adults with AD, and institutionalization is often the result because caregivers are burdened and exhausted from the demands of around-the-clock care.
Sustained Use of CPAP Slows Deterioration of Cognition, Sleep, and Mood in Patients with Alzheimer’s Disease and Obstructive Sleep Apnea: A Preliminary Study

Jana R. Cooke, M.D.1,2; Liat Ayalon, Ph.D.2; Barton W. Palmer, Ph.D.2; Jose S. Loredo, M.D.1,2; Jody Corey-Bloom, M.D., Ph.D.4,5; Loki Natarajan, Ph.D.2; Lianqi Liu, M.D.2; Sonia Ancoi-Izrael, Ph.D.2
You can’t help getting older, but you don’t have to get old.

[GEORGE BURNS]