Northern Light Health

SLEEP

Implications for healthy aging

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Nothing to disclose.

Overview

Sleep physiology in older adults

Health implications of sleep disorders

Behavioral health implications of sleep disorders

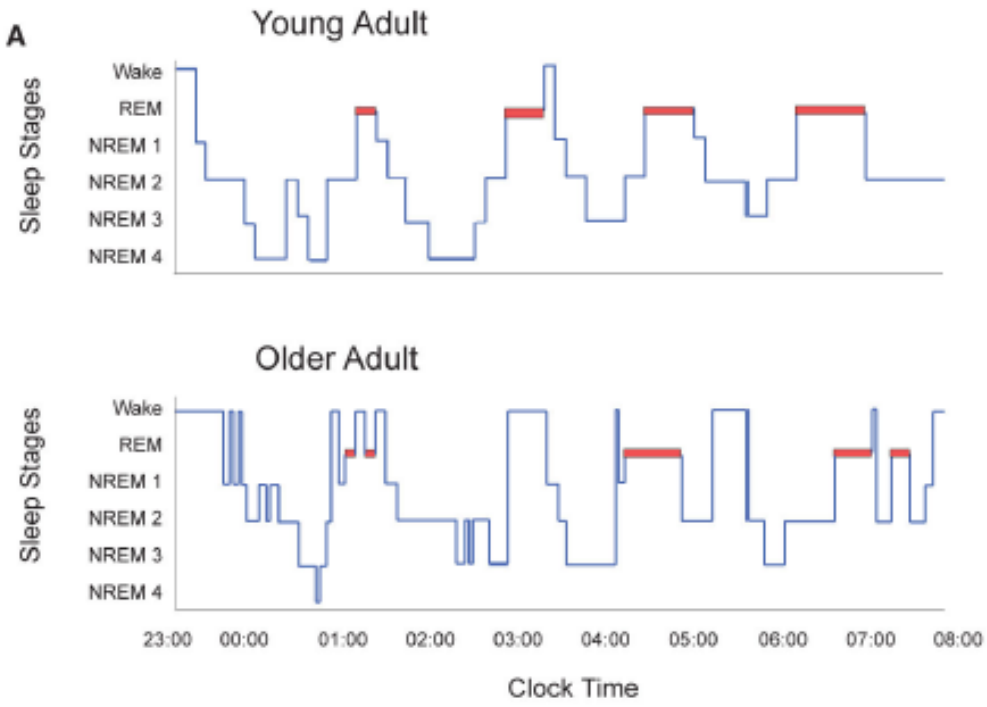
Clinical assessment of sleep

Insomnia, hypersomnia and parasomnia

Treatment of insomnia in older adults and those with dementia

Sleep and Human Aging

Mander BA et al Neuron 2017

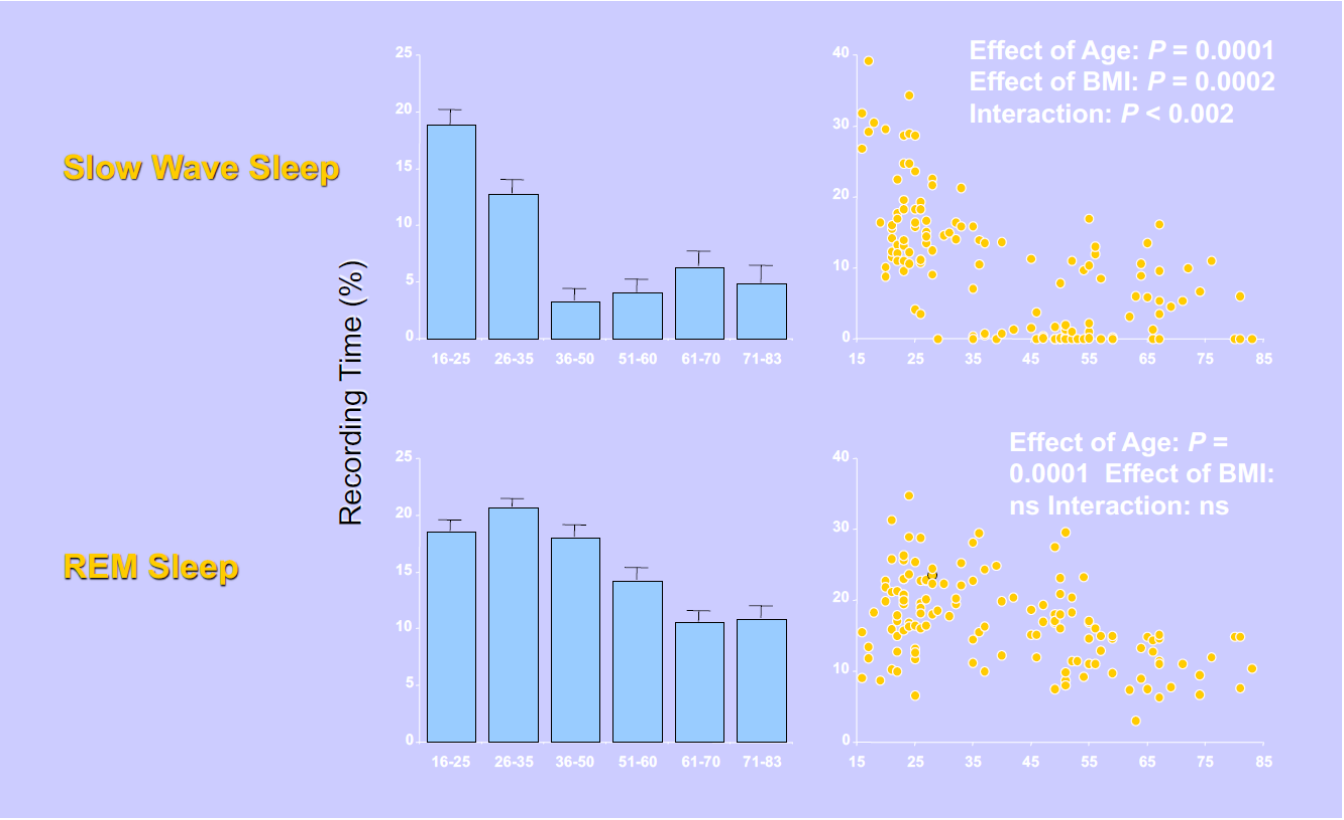


Lower sleep efficiency
More awakenings
More daytime sleep
Less SWS (M<F)
Decreased sleep spindles
Longer sleep latency
Phase advance and reduced amplitude of rhythm in sleep, melatonin

Sleep is highly variable from person to person and influenced by **co-morbid conditions and cortical atrophy**

Aging Effects on SWS and REM

Van Cauter et al. JAMA 2000



Do Older Adults Sleep Less?

National Sleep Foundation Poll (www.sleepfoundation.org)

Percent Reporting the Number of Hours Slept on Weeknights (past two weeks)

	Age				Gender	
	18-54*	55-84	55-64	65-84	Older Men	Older Women
n=	(701)	(1,506)	(631)	(849)	(634)	(872)
Less than 6 hours	16%	13%	14%	12%	11%	14%
6 to 6.9 hours	25	21	24	20	23	20
7 to 7.9 hours	30	28	30	25	30	26
8 to 8.9 hours	21	28	25	29	26	28
9 or more hours	6	7	5	8	7	7
Mean (# of hours)	*6.7*	*7.0*	*6.9*	*7.1*	*7.0*	*7.0*
Median (# of hours)	*7.0*	*7.0*	*7.0*	*7.0*	*7.0*	*7.0*

**Percent Reporting the Number of Hours Slept on Weekends (past two weeks)*

	Age				Gender	
	18-54*	55-84	55-64	65-84	Older Men	Older Women
n=	(701)	(1,506)	(631)	(849)	(634)	(872)
Less than 6 hours	10%	11%	11%	10%	10%	11%
6 to 6.9 hours	12	17	16	17	19	15
7 to 7.9 hours	22	28	30	26	29	28
8 to 8.9 hours	33	32	32	32	31	33
9 or more hours	22	9	9	9	9	8
Mean (# of hours)	*7.6*	*7.1*	*7.1*	*7.2*	*7.1*	*7.2*
Median (# of hours)	*8.0*	*7.0*	*7.0*	*7.0*	*7.0*	*7.0*

**2002 Sleep in America poll*

**2002 Sleep in America poll*

Sleep Efficiency and Aging
Bixler EO et al. J Clin Metab 2005

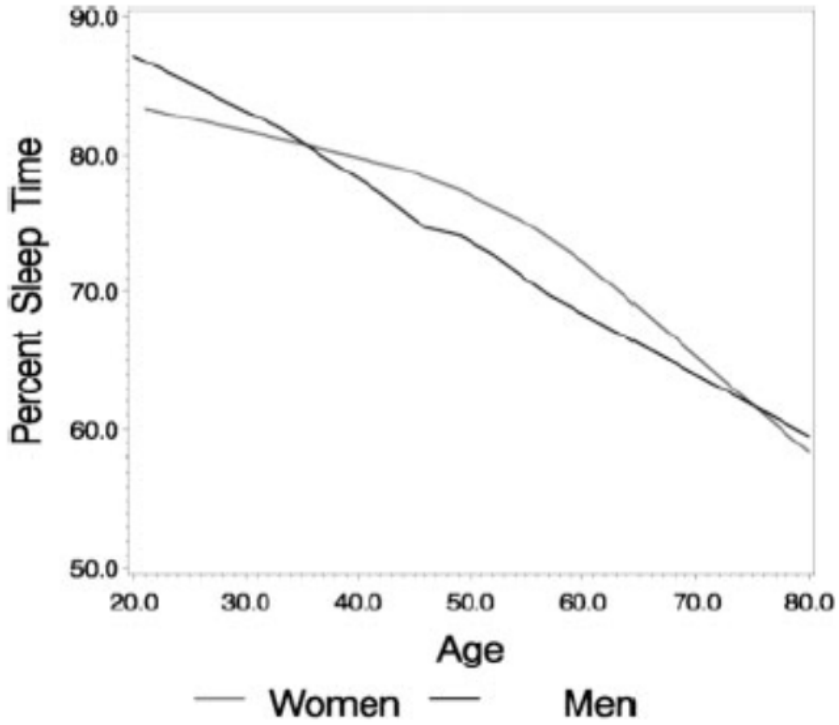


FIG. 5. Age-specific prevalence of % ST in subjects without a complaint of sleep disturbance.

Frequency of Sleep Complaints
Foley DJ et al. Sleep 1995

A survey of >9,000 older adults in 3 communities

23-34% endorsed symptoms of insomnia

7-15% “never feel” rested upon awakening

Sleep complaints associated with:

respiratory symptoms, physical disability, **depressive symptoms** and poorer self-perceived health

Napping in 24.6% (under-report?)

Risk of Sleep Disturbances

Smagula SF et al. Sleep Med Rev 2016

Review of 21 population-based prospective studies of emerging sleep disturbance:

Age-itself not an independent predictor

Strongest predictors: female sex, **depression**, physical illness

Weaker associations: lower activity level, lower socioeconomic status, inflammatory markers, cognitive impairment

Sleep and Mental Health in Old Age

- WASO and DST/Naps correlated with depression in study of 3045 older women (Maglione JE et al. JAGS 2012)
- Insomnia is more common in anxious and depressed older adults vs. controls (35% vs. 18%) (Leblanc MF et al. 2015)
  - Prolonged sleep onset latency predictive of anxiety vs. depression
- Large meta-analysis of insomnia and risk of subsequent depression, found RR=2.27 (CI=1.9-2.7) (Li L et al. 2016)
- Poor sleep quality associated with higher risk of depression relapse (Reynolds C et al. NEJM 2006)

Sleep and Inflammation in Aging
Irwin MR Interface Focus 2014

Sleep deprivation increases cellular and genomic markers of inflammation, including IL-6, TNF-α,CRP

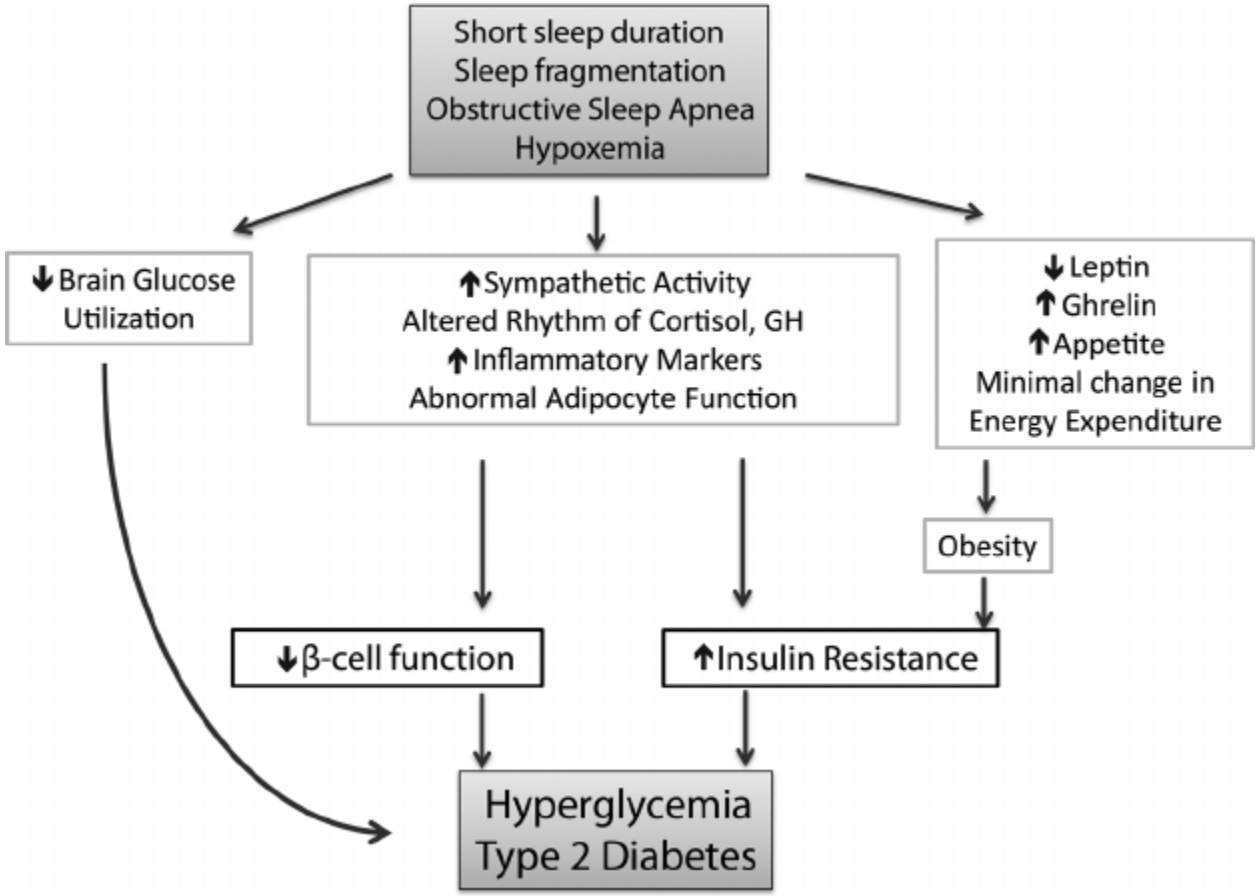
Sleep loss also upregulates multiple genes involved in inflammatory responses

These markers are associated w risk of depression and disability in old age

Studies of CBT-I have documented reductions in inflammatory markers

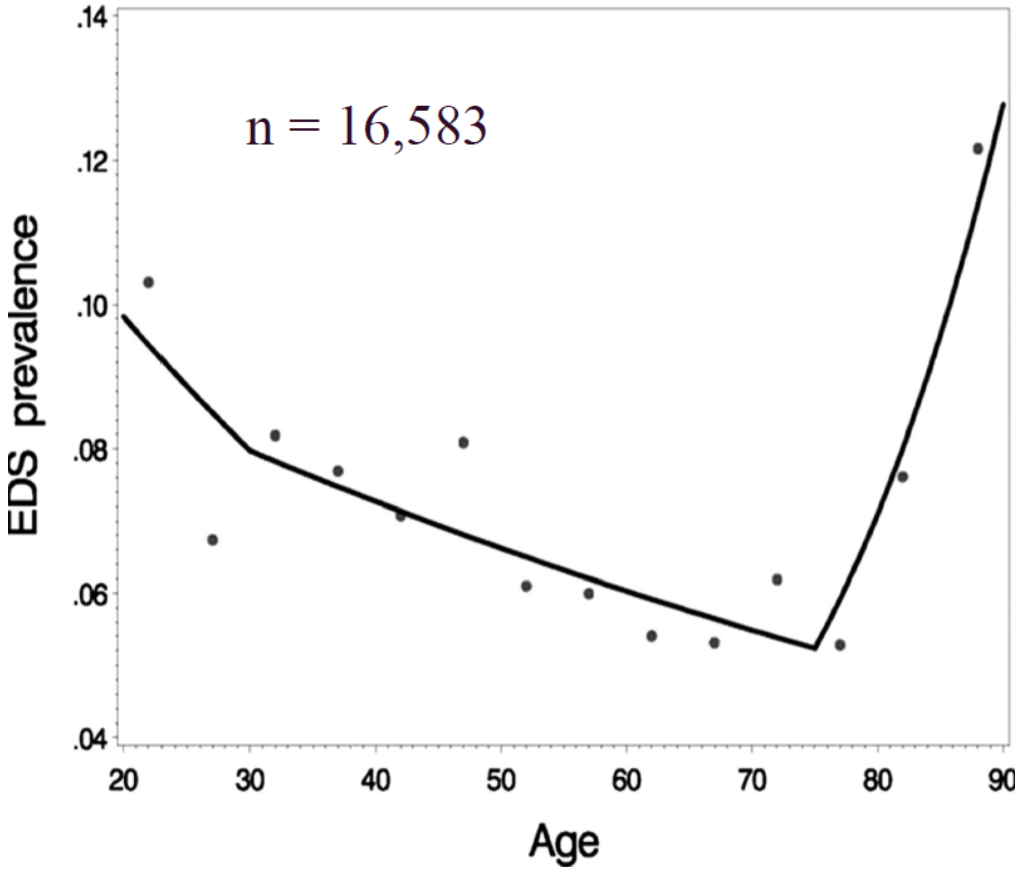
Sleep and Metabolism

Reutrakul S and Van Cauter E Ann NY Acad Sci 2014



Excessive Daytime Sleepiness and Age

Bixler EO et al. J Clin Endo Metab 2005



Excessive Daytime Sleepiness

True EDS is common but not a normal part of aging

EDS can be due to age-associated conditions:

Pain, medications, AHI>20, depression, diabetes, insomnia, COPD (Gooneratne NS Sleep 2012)

EDS associated w a 33% increased likelihood of decline in MMSE over 8 yr. period in large population-based study (Jaussent I et al. Sleep 2012)

Sleepiness and AD Biomarker
Spira A et al. Sleep 2018

Association of Baseline Excessive Daytime Sleepiness with Aβ+ Status (PiB PET) 15.7 ±3.4 years later

	n (%) Aβ+	Unadjusted OR (95% CI) *p*-value	MV-adjusted* OR (95% CI) *p*-value
EDS+	17 (56.7)	3.37 (1.44, 7.90) $p = 0.005$	2.75 (1.09, 6.95) $p = 0.033$
EDS-	26 (28.0)	1.00 (ref)	1.00 (ref)

N = 123. *Adjusted for age, age^2, sex, education, body mass index.
Aβ+ = [^{11}C] Pittsburgh compound B cortical distribution volume ratio >1.06.

Spira et al., September 5, 2018, *SLEEP.*

Sleep Apnea

Gildeh N et al. J Thorac Dis 2016

Highly prevalent (22% in men, 17% in women)

Causes intermittent hypoxia leading to:

Systemic hypertension

Systemic inflammation

Cognitive impairment

Metabolic syndrome

Renal disease

Accidents

Cancer

SDB more common in older adults, but less daytime sleepiness:

More fatigue and cognitive impairment

SDB and Cognition
Spira A et al. JAGS 2008

Cross sectional study of older women (N=400, mean age 82.8 yrs.)

Likelihood of impairment on MMSE:

- AHI>15: OR=1.4 (CI 1.0-1.9)
- AHI>30: OR=3.4 (1.4-8.1)
- SaO2 nadir<80%: OR=2.7 (1.1-6.6)

Each SD unit increase in AHI increased odds of CI by 70%

Prospective study by Yaffe K et al. JAMA 2011:

- AHI>15 nearly doubled risk of MCI or dementia over 5 years

Very high prevalence of SDB in AD: 50% have AHI>20

Some evidence that treatment w CPAP slows progression (Ancoli-Israel S et al. JAGS 1991)

Screening Questionnaires for OSA
Amra B et al. Oman Med J 2018

All scales had acceptable sensitivity to moderate and severe OSA (AHI>15 or 30)in sleep clinic populations

AASM recommends against relying only on questionnaires for diagnosis (Kapur VK et al. J Clin Sleep Med 2017)

STOP-Bang Questionnaire may have best sensitivity

>97% for both mild and severe including >65 (Arsian BO et al. 2020)

Epworth Sleepiness Scale has good sensitivity for severe OSA, but EDS less reliable symptom in older adults

Parasomnia: REM Behavior Disorder

Boeve BF Ann NY Acad Sci 2010

RBD: vivid dreams w complex motor activity during REM sleep

REM w/o muscle atonia

Dream enactment behaviors

Associated w α-synucleinopathy (LBD, PD, MSA): Majority of cases but may be seen in others

RBD may predate onset of motor or cognitive symptoms (average 12.7 years)

DDx: OSA, other parasomnias, nocturnal seizures

Treated w clonazepam (0.25-2 mg) or melatonin (3-12 mg). (Jung Y and St. Louis EK Current Treat Options Neurol 2016)

Restless Legs Syndrome

Core feature: distressing, irresistible need or urge to move one's legs (akathisia in legs) to relieve the uncomfortable feeling, coming on with rest and relieved with movement (Early CJ NEJM 2003)

Prevalence in general population of 2.5-15% with an age-associated increase in prevalence

Often associated with PLMs/myoclonus

Chronic, can worsen in time and generalize to upper body

Treatment (During EH and Winkelman JH, Drugs and Aging 2019) :

Moderate exercise, avoid EtOH, stretching before bed, acupuncture, vibration, Fe++ (when iron stores are low), medications (dopamine agonists, gabapentin, pregabalin, opioids, BZ and BZRA??

Insomnia Disorder

Diagnostical and Statistical Manual of Mental Disorders, Fifth Edition, American Psychiatric Press 2013

Primary

Difficulty initiating sleep

Difficulty maintaining sleep

Early morning awakening with inability to return to sleep

Secondary

The sleep disturbance causes clinically significant distress or impairment

Occurs at least 3 nights per week

Is present for at least 3 months

Occurs despite adequate opportunity for sleep

Cannot be explained by and does not occur exclusively during the course of another sleep-wake disorder

Is not attributable to the physiological effects of a drug of abuse or medication

Coexisting mental disorders and medical conditions do not adequately explain the predominant complaint of insomnia

Insomnia as a Geriatric Syndrome
Vaz Fragoso and Gill JAGS 2007

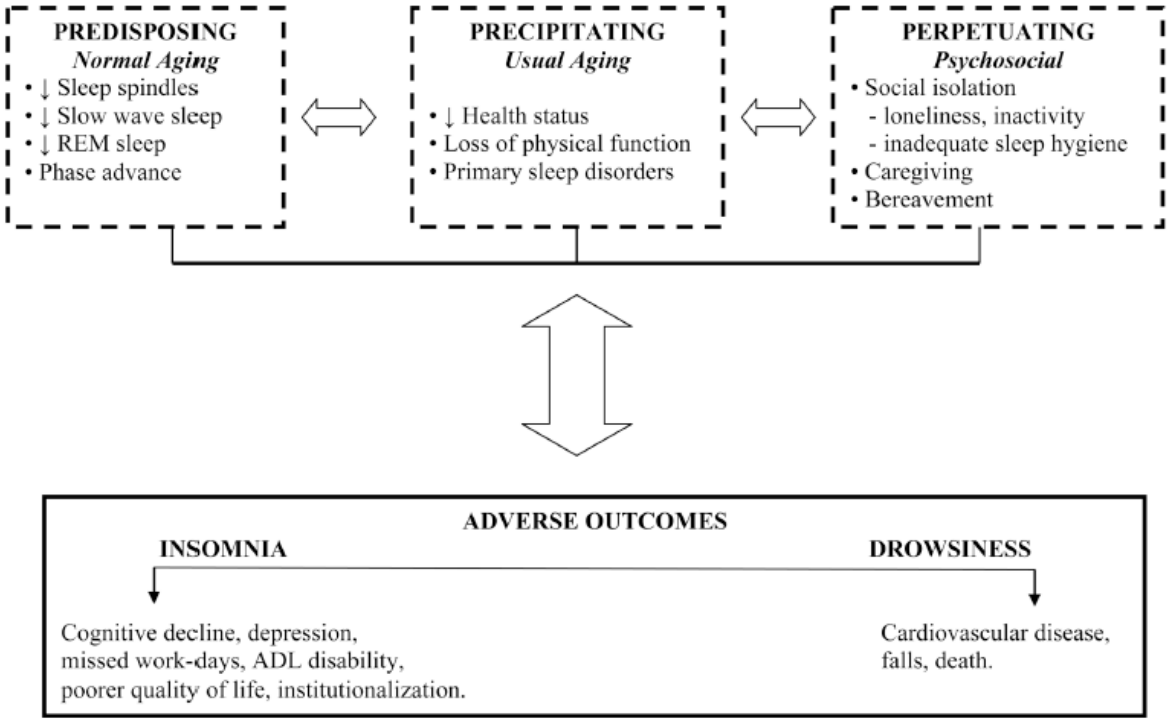


Figure 1. Mechanisms underlying sleep complaints and associated adverse outcomes
Adapted from an insomnia model previously described by Spielman and colleagues.[46] Sleep complaints present as various combinations of insomnia and drowsiness, and are a consequence of multiple predisposing, precipitating, and perpetuating factors. The postulated relationships are interdependent, as denoted by the bi-directional arrows, and are characterized by interindividual variability, as denoted by the dashed boundaries. See text for discussion.

Epidemiology of Insomnia in Older Adults

Miner B et al. JAGS 2018

Community sample (N=379, mean age 84.3, 68% F)

High medical co-morbidities

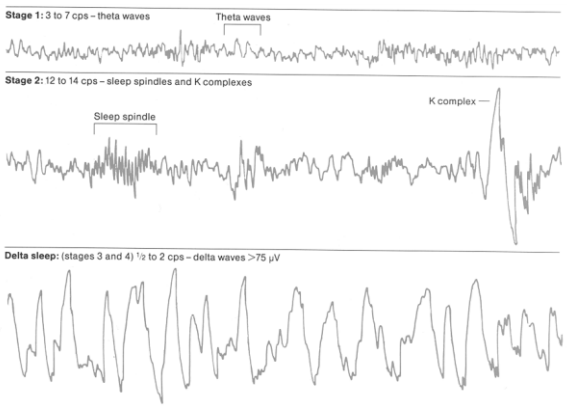
Used Insomnia Severity Index: mild 8-14, moderate 15-21, severe 22-28

43% >8 on ISI, mean 12.3 (mild-moderate)

Strongest correlation w depression (OR=8.3!!) and RLS (OR=2.5)

Clinical Assessment of Insomnia

- Polysomnography
- Wrist actigraphy
- Wearables
- Sleep diaries
- Sleep rating scales



Name_____ Date_____

Sleep Quality Assessment (PSQI)

What is PSQI, and what is it measuring?

The Pittsburgh Sleep Quality Index (PSQI) is an effective instrument used to measure the quality and patterns of sleep in adults. It differentiates "poor" from "good" sleep quality by measuring seven areas (components): subjective sleep quality, sleep latency, slee duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications, and daytime dysfunction over the last month.

INSTRUCTIONS:

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions.

During the past month,

1. When have you usually gone to bed?
2. How long (in minutes) has it taken you to fall asleep each night?
3. What time have you usually gotten up in the morning?
4. A. How many hours of actual sleep did you get at night?
   B. How many hours were you in bed?

	Not during the past month (0)	Less than once a week (1)	Once or twice a week (2)	Three or more times a week (3)
A. Cannot get to sleep within 30 minutes				
B. Wake up in the middle of the night or early morning				
C. Have to get up to use the bathroom				
D. Cannot breathe comfortably				
E. Cough or snore loudly				
F. Feel too cold				
G. Feel too hot				
H. Have bad dreams				
I. Have pain				
J. Other reason (s), please describe, including how often you have had trouble sleeping because of this reason (s):				
6. During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?				
7. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?				
8. During the past month, how much of a problem has it been for you to keep up enthusiasm to get things done?				
9. During the past month, how would you rate your sleep quality overall?	Very good (0)	Fairly good (1)	Fairly bad (2)	Very bad (3)

TWO WEEK SLEEP DIARY

INSTRUCTIONS:
1. Write the date, day of the week, and type of day: Work, School, Day Off, or Vacation.
2. Put the letter "C" in the box when you have coffee, cola or tea. Put "M" when you take any medicine. Put "A" when you drink alcohol. Put "E" when you exercise.
3. Put a line (|) to show when you go to bed. Shade in the box that shows when you think you fell asleep.
4. Shade in all the boxes that show when you are asleep at night or when you take a nap during the day.
5. Leave boxes unshaded to show when you wake up at night and when you are awake during the day.

SAMPLE ENTRY BELOW: On a Monday when I worked, I jogged on my lunch break at 1 PM, had a glass of wine with dinner at 6 PM, fell asleep watching TV from 7 to 8 PM, went to bed at 10:30 PM, fell asleep around Midnight, woke up and couldn't go back to sleep at about 4 AM, went back to sleep from 5 to 7 AM, and had coffee and medicine at 7:00 in the morning.

Today's Date	Day of the week	Type of Day Work, School, Off, Vacation	Noon	1PM	2	3	4	5	6PM	7	8	9	10	11PM	Midnight	1AM	2	3	4	5	6AM	7	8	9	10	11AM
sample	Mon.	Work		E					A				I									C M				

week 1

week 2

Epworth Sleepiness Scale

Name: _____

Date: _____

Your age: (Yr) _____ Your sex: ❑ Male ❑ Female

How likely are you to doze off or fall asleep in the situations described below, in contrast to feeling just tired?

This refers to your usual way of life in recent times.

Even if you haven't done some of these things recently try to work out how they would have affected you.

Use the following scale to choose the most appropriate number for each situation:-

0 = would never doze
1 = Slight chance of dozing
2 = Moderate chance of dozing
3 = High chance of dozing

Situation	Chance of dozing
Sitting and reading	
Watching TV	
Sitting, inactive in a public place (e.g. a theatre or a meeting)	
As a passenger in a car for an hour without a break	
Lying down to rest in the afternoon when circumstances permit	
Sitting and talking to someone	
Sitting quietly after a lunch without alcohol	
In a car, while stopped for a few minutes in the traffic	
Total	

Score:
0-10 Normal range
10-12 Borderline
12-24 Abnormal

Clinical Approach to Insomnia
Adapted from AGS Geriatrics E&M Tools ©2018

Screening Questions:

Satisfied w sleep?
Sleepy or fatigued during the day?
Stay awake for an hour as a passenger in a car?
Can read or watch TV in afternoon for 30 min. w/o dozing?
Bedpartner report loud snoring, interrupted breathing or excessive movements?

Insomnia symptoms?
Move on to insomnia DDx

Parasomnia or Hypersomnia?
Consider Sleep lab referral

Clinical Approach to Insomnia
Adapted from AGS Geriatrics E&M Tools ©2018

Insomnia: Insufficient or nonrestorative sleep?

Clarifying questions:

Effect on daytime function? How much sleep do you need? Lights out time? Time to fall asleep? Time awake? Symptoms during the night? Restless legs? Number of awakenings?

Objective data:

Actigraphy

Sleep log/diary

http://sleepeducation.org/docs/default-document-library/sleep-diary.pdf?sfvrsn=2

https://www.nytimes.com/wirecutter/reviews/best-sleep-tracking-app/

Insomnia: Comorbid Factors

Adapted from AGS Geriatrics E&M Tools ©2018

- Mental health
- Neurologic
- Cardiovascular
- Gastrointestinal
- Musculoskeletal
- Urologic (nocturia)
- Drugs
- Substance use

Wholistic Approach to Insomnia

CBT-I/BBT-I: **Bed restriction**, stimulus control, sleep hygiene, increased daytime activity, evening rituals

Bright light exposure:

AM BL and PM MLT for delayed sleep phase (night owls)

PM BL for advanced sleep phase (morning larks)

Treat comorbid conditions (RLS, pain, GERD, depression, anxiety)

Cognitive Behavioral Therapy for Insomnia

Adapted from the AGS Geriatric Evaluation and Management Tool for Insomnia

Intervention	Goal	Brief Description
Stimulus control	To recondition maladaptive sleep-related behaviors	Patient is instructed to go to bed only when sleepy, not use the bed for eating or looking at monitors (eg, television, laptops, tablets), get out of bed if unable to fall asleep, return to bed only when sleepy, get up at same time each morning, not take naps during the day
Sleep restriction	To improve sleep efficiency (time asleep over time in bed) by limiting time in bed	Patient first keeps a sleep diary for 1–2 weeks to determine average total daily sleep time, then stays in bed only that amount of time plus 15 minutes; gets up at same time each morning; takes no naps during the day; gradually increases time allowed in bed as sleep efficiency improves
Cognitive interventions	To change misunderstandings regarding sleep	Patient's dysfunctional beliefs and attitudes about sleep are identified; patient is educated to change these beliefs and attitudes, including both normal changes in sleep with age and changes that are pathologic

RCT of CBT-I in Post-menopausal Women
Drake CL et al. Sleep 2019

43-48% of PMW complain of insomnia

Drake et al. randomized 150 PMW (mean age=56.4) to CBT-I, sleep restriction therapy (SRT) or sleep hygiene education (SHE)

mean SE=71%, WASO=57.7 min. and ISI score=15.2 (>11=clinical insomnia) at BL

CBT-I: Six weekly in–person sessions w comprehensive cognitive and behavioral components (including SRT, SHE) by RN specialist in behavioral sleep medicine

SRT: Two wk. protocol of prescribed bed schedule also overseen by RN sleep specialist by in-person and phone

SHE: minimal intervention control of 6 weekly emails on sleep and sleep hygiene

Results of RCT of CBT-I in PMW

Drake CL et al. Sleep 2019

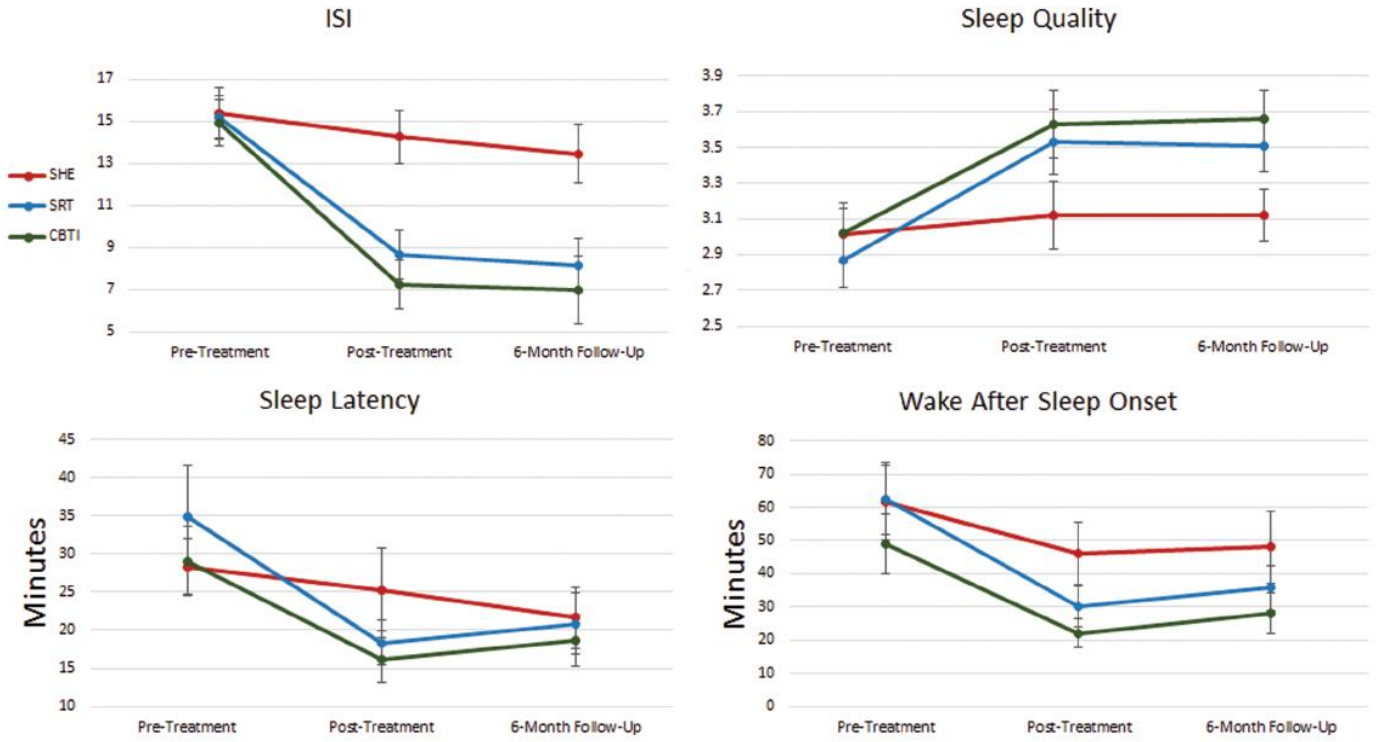


Figure 2. Treatment effects of CBTI, SRT, and SHE on global insomnia, sleep quality, sleep latency, and wake after sleep onset.

RCT of CBT-I Using "Sleep Coaches"

Alessi C et al. JAGS 2016

Community dwelling older veterans w >3 mos. insomnia

Non-clinical sleep coaches delivered a 5-session manual-based CBT-I course in small groups with weekly supervision.

Controls received 5 sessions of general sleep education.

Sleep diaries and actigraphic outcomes:

Improved sleep latency, daytime wake time and sleep efficiency at BL, 6 and 12 mos.

Internet Resources and Apps

Prescription services: Include telehealth diagnostic evaluation by sleep specialist and CBT/BBT guided interventions

Subscription services: Self-assessment and sleep coaches guide user through CBT/BBT and on-line resources

Sleep hygiene and relaxation/meditation aids

NAPS: Yay or Nay?

Napping in Older Adults

Napping is under-reported, but very common

39% (65-74) and 46% (75-84) reported napping (National Sleep Foundation, 2003)

Associated w sleep fragmentation (OR 2.1), SDB (OR 2.4), diabetes (OR 6.1), pain (OR 2.2) (Goldman SE et al. Sleep 2008)

Daytime sleep >1 hr. associated w age, poor health status and cognitive decline (Leung Y et al. J Gerontol Biol Med Sci 2018)

Prescribed napping improves daytime cognition and does not affect nighttime sleep; N=22, mean age 70. (Campbell S et al. JAGS 2011)

Adherence better w 45 min. than 2 hr. nap prescription

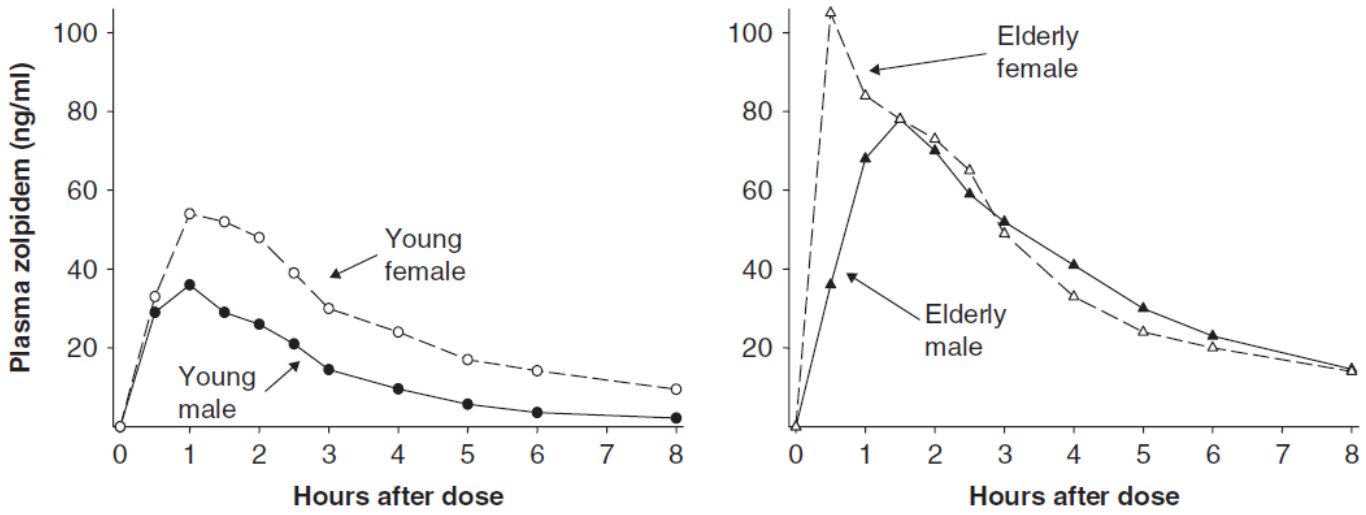
Another study showed day or evening nappers still slept at night (Dautovich ND et al. Sleep 2008)

Medications for Insomnia
Adapted from AGS Geriatrics E&M Tools ©2018

MEDICATIONS USED FOR INSOMNIA IN OLDER ADULTS				
Class, Medication	Starting Dose (Mg)	Usual Dose (Mg)	Half-Life (Hours)	Comments
Intermediate-acting benzodiazepine				
Temazepam	7.5	7.5–30	8.8	Psychomotor impairment, increased risk of falls
Short-acting non-benzodiazepines				
Eszopiclone	1	1–2	6	Reportedly effective for long-term use in selected individuals; may be associ.ated with unpleasant taste, headache; may cause next-day mental impairment, risk of falls; avoid administration with high-fat meal
Zaleplon (a pyrazolopyrimi-dine)	5	5–10	1 (reportedly un-changed in older adults)	Can cause daytime drowsiness and dizziness; risk of falls
Zolpidem (an imidazopyridine)	5	5	1.5–4.5 (3 in older adults; 10 in hepatic cirrhosis)	Reportedly little daytime carryover, tolerance, or rebound insomnia; complicated sleep behaviors/parasomnias have been reported; risk of falls
Melatonin receptor agonist				
Ramelteon	8	8	1.5 (2.6 in older adults)	Dizziness, myalgia, headache, other adverse events reported; no significant rebound insomnia or withdrawal with discontinuation
Sedating antidepressants				
Mirtazapine (off-label)	7.5	7.5–45	31–39 in older adults; 13–34 in younger adults; mean = 21	Increased appetite, weight gain, headache, dizziness; daytime carryover; used for insomnia with depression; more sedating at lower doses than higher doses
Trazodone (off-label)	25–50	25–150	Reportedly 6 ± 2; prolonged in older adults and obese individuals	Moderate orthostatic effects; effective for insomnia with depression; risk of falls

Zolpidem Pharmacokinetics

Grennblatt DJ and Roth T Expert Opinion Pharmacother 2012



Higher peak plasma levels and slower elimination increase risk of acute side effects in older adults: ataxia, confusion, parasomnia

Sleep Meds and Risk of MCI/Dementia

Burke SL et al. Sleep Medicine 2018

Analyzed NACC UDS of 6798 subjects

With and without subjective sleep disturbance

APOe4 status and use of BZRA or trazodone

Analyzed for risk of progression to MCI

Found that reported "sleep disturbance" increased risk of MCI but sleep medication mitigated risk regardless of APOe4 status

A recent review of BZRA and dementia risk also failed to find evidence of increased risk (Kaufman CN et al. 2020)

But data are mixed: Others report risk of MCI/dementia w BZ for sleep is increased(Ettcheto M et al. 2019) but other risk factors influence risk (Shih HI et al. 2015)

Suvorexant in Older Patients w Insomnia

Herring WJ et al. Am J Ger Psychiatry 2017

Suvorexant, a dual orexin receptor antagonist (DORA)

Blocks orexin A and B receptors

Sub-analysis of data for 319 subjects >65 from a previously published Phase III study

Self reports and PSG data showed improvements in SOL and WASO at week 1, month 1 and month3, with slight reductions in treatment effects over time

Somnolence was most common AE (8.8% at 30 mg, 5.4% at 15 mg and 3.2% for PLB) due to long ½ life?*

- * Clinical starting dose is 10 mg with max. of 20 mg

Newer agent (lemborexant) also shown to be effective in >55 yrs.

(Rosenberg R et al. JAMA Network Open 2019)

Effects of AD on Sleep

Tractenberg R and Singer C J Sleep Res 2005

AD (n=263) Patients vs. Non-AD Seniors (n=399):

Spend more time in bed

Have much more daytime sleep

Have less nighttime sleep

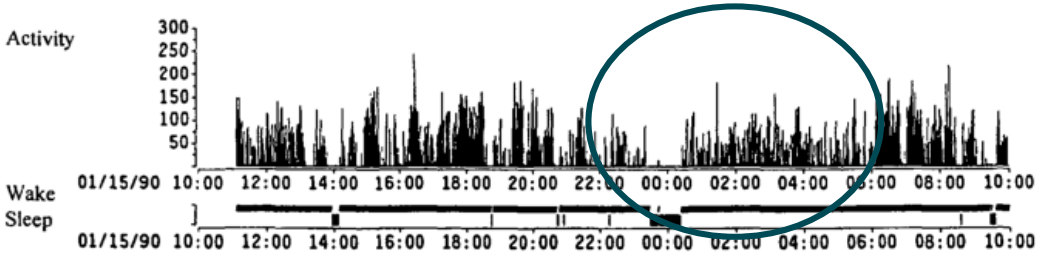
Exaggeration of normal age-related sleep

Worsening dementia associated w more daytime sleep and nighttime sleep fragmentation

PSG studies show less SWS, REM w dementia severity (Bliwise D et al. Sleep 1993)

Rest/activity Fragmentation in Dementia

a. Demented patient



b. Non-demented patient

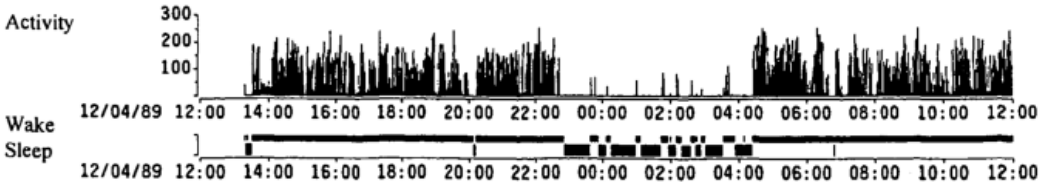


FIG. 1. Activity plot of a nursing-home patient with severe sleep fragmentation. There were no long intervals of consolidated wake or sleep.

Ancoli-Israel et al., Sleep 1997;20:18-23. (p. 20)

More nighttime activity and daytime microsleeps. Different than "sundowning".

Sleep Fragmentation and Incident AD

Lim ASP et al. Sleep 2013

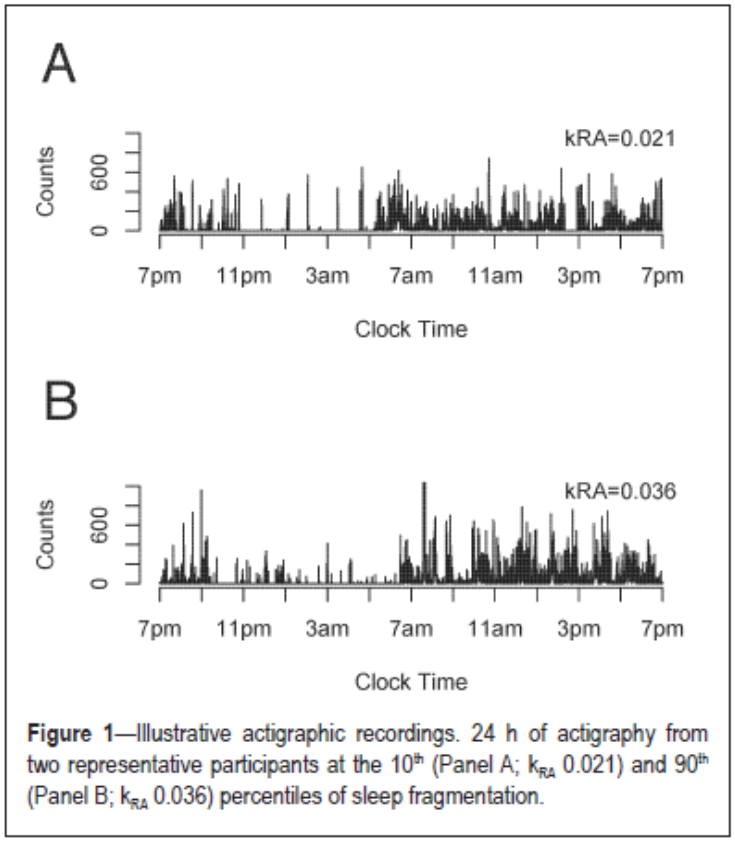


Figure 1—Illustrative actigraphic recordings. 24 h of actigraphy from two representative participants at the 10th (Panel A; k_{RA} 0.021) and 90th (Panel B; k_{RA} 0.036) percentiles of sleep fragmentation.

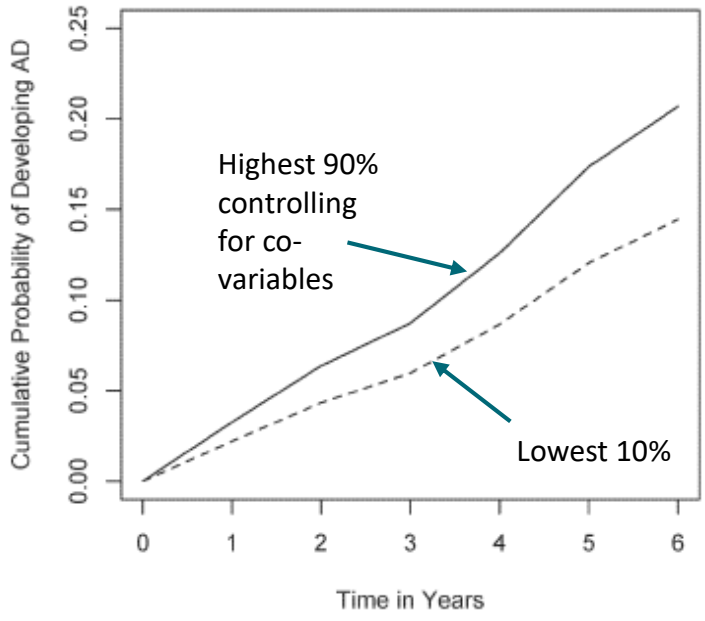


Figure 2—Expected risk of AD. The model predicted risk of AD based on the entire cohort is illustrated for two hypothetical average participants with high (Solid line: 90th percentile; k_{RA} = 0.036) and low (Dotted line: 10th percentile; k_{RA} = 0.021) levels of sleep fragmentation.

N=737

Rush Memory and Aging Project, Avg. f/u 3.3 yrs.

Sleep Duration and β-amyloid

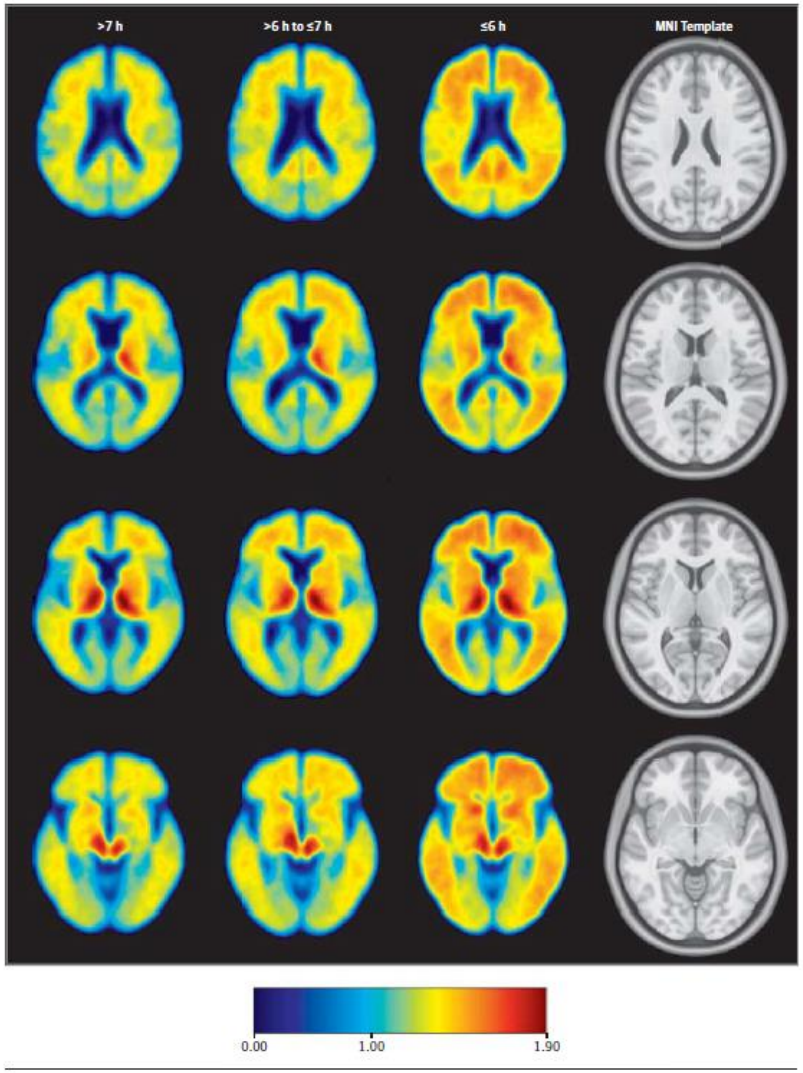
Spira A et al. JAMA Neurol 2013

Sleep disruption associated w worse cognitive outcomes and risk for AD

Animal models show increased amyloid plaque deposition with less sleep

In this study of 70 subjects from the BLSA, self-reported sleep duration <6 hrs. was associated with more β-amyloid on PET

Figure. Unadjusted Distribution Volume Ratios (DVRs) of Carbon 11–Labeled Pittsburgh Compound B Positron Emission Tomography Images by Sleep Duration



Sleep Duration and Cognitive Decline

McSorley VE et al. A J Epidemiology 2019 188:6:1066-75

Investigators studied sleep w wrist-actigraphs and self-report and cognitive function (MoCA); N=759

Low sleep continuity (more WASO) confirmed w actigraphs: 43% greater risk of cognitive decline over 5 years.

Sleep duration and cognitive function: sleep times <7 hrs. and >8 or 9 hrs. both associated with CI (Alfini AJ et al. Current Opin Behav Sci 2020)

Summary of Sleep AD Interactions
Cedernaes J et al Sleep Med Rev 2017

Observational studies: higher risk of cognitive decline and AD pathology in people with insomnia in mid-life

Each additional symptom of insomnia increases risk of MCI/dementia by 5% (Resciniti NV et al. 2021)

Experimental sleep disruption increases levels of pathologic proteins, increases inflammation/oxidative stress

More AD pathology in those with less sleep

Sleep fragmentation and incident insomnia increase risk

People with AD show further deterioration in sleep, wake and circadian fragmentation-major factor in caregiver stress

Pharmacotherapies for Sleep in AD

McCleeryJ et al. Cochrane Database 2014; 21:3

Few RCTs: melatonin (2), trazodone (1) and ramelteon (1)

Melatonin showed non-significant trends for more nighttime sleep and less daytime sleep

Melatonin was favored vs. placebo in subjective assessments by caregivers, n=157 (Singer C et al. 2003)

Trazodone associated w improved sleep efficiency and slowed rate of decline in a small study (La AL et al. J Alz Dis 2019)

RCT of Non-Pharm Interventions to Improve Sleep-Wake in NH Residents

Alessi CA et al. JAGS 2005

339 of 492 NH residents screened had EDS

Of those, 133 had disrupted nighttime sleep

Intervention: Five days of intervention w ≥30 min. of daily sunlight exposure, ↑daytime activity, ↓daytime TIB, ↓ nighttime noise and light

~30% reduction in daytime sleep episodes but only small trend in more nighttime sleep

Increased social interactions and conversation

6/06/2021

Light Exposure and Sleep in AD

Figueiro M. Neurodegenerative Disease Management 2017

Human SCN dependent on circadian light cues

May become desynchronized with day/night cycle w inadequate exposure to light/dark cycle

Evening light exposure before the middle of the night body temperature nadir phase delays; early AM light after the BT nadir phase advances

Older adults and those w ADRD:

Reduced circadian rhythmicity in sleep and wake

Reduced exposure to chronobiologic ambient light

Lower daytime light exposure associated with lower daytime activity levels and higher nighttime activity levels

BL interventions generally:

- increase circadian variables in sleep and wake (either amplitude, stability or both) but not in all studies and show less benefit w agitation in evening
- May improve outcomes in delirium (Sien Chong M et al. Clin Interv Aging 2013)

Since circadian systems adjusts to previous light exposure, lower levels of light intensity that is better tolerated may be more effective

Rejoice! The End of Slides.

Q&A