Healthy Sleep, Healthy Brain – Mechanisms, Diagnosis, and Treatment

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One Thursday afternoon in 2024 in the geriatrics clinic…

Beatrice’s story

- 76 year-old woman
- 5 years of difficulties staying asleep at night, accompanied by excessive daytime sleepiness
- 1 year of increasing memory difficulty
- Gets very tired during the day – especially after dinner
- Some days goes to bed as early as 7-8PM but many days will force herself to stay awake until 11PM for social reasons
- Falls asleep quickly, but wakes up 4-5 times a night then wakes up at 4AM most mornings, unable to get back to sleep → begins her day
- Over last year, increasing memory difficulties – forgetting where she placed her keys, or forgetting what she had gone into a store to buy

Beatrice's Questions

1. What is causing my sleep difficulties? How can we figure this out?
2. I'm worried about my memory difficulties. Are these at all related to my difficulties with sleep?
3. What can I do to improve my sleep? Will improving my sleep help my memory and prevent dementia?

Question 1: What is causing my sleep difficulties? How can we figure this out?

Possible Contributors to Beatrice's Sleep Difficulties

1. Circadian Rhythm Dysfunction (+ insomnia)?

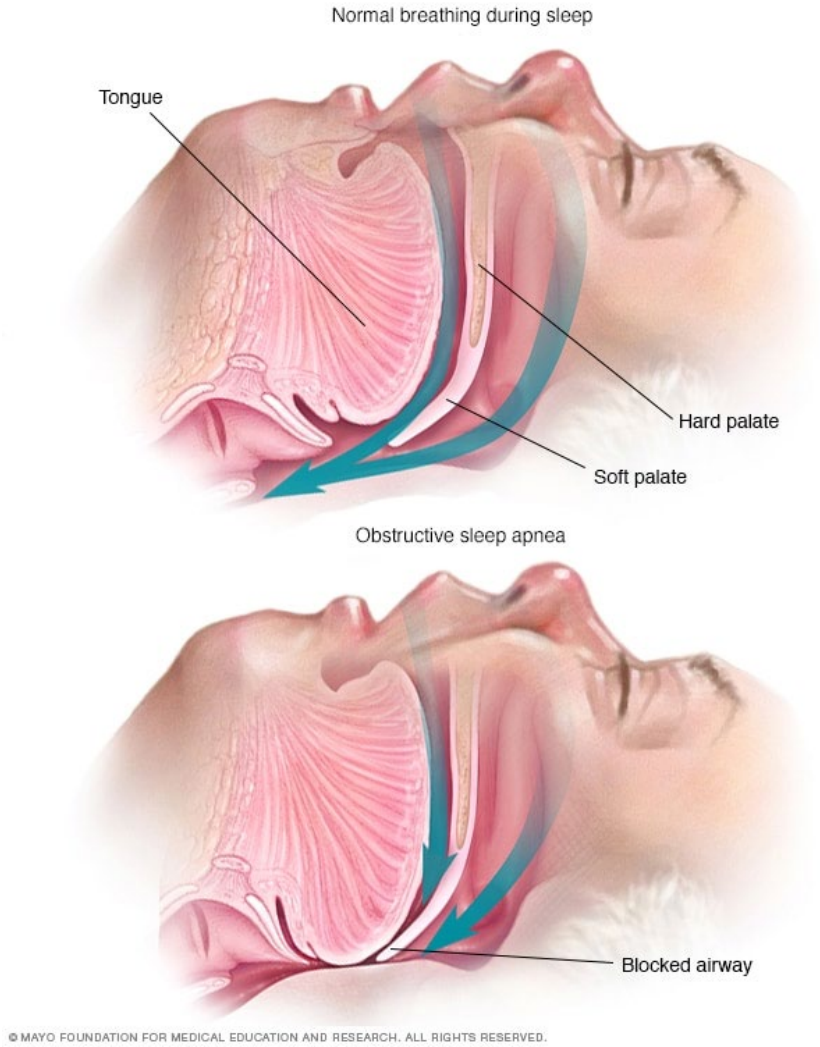
2. Sleep apnea (snoring)

3. Age- and neurodegeneration- related damage to sleep regulatory areas (age)

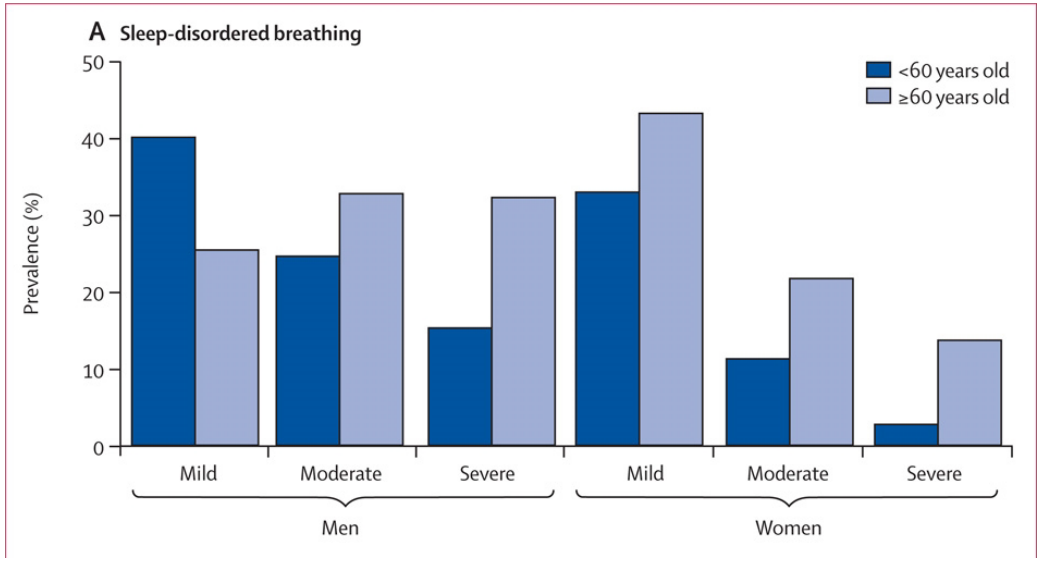
Insomnia and Circadian Rhythm Dysfunction – Dr. Dang-Vu

Sleep Apnea

What is Sleep Apnea



- Obstructive sleep apnea is characterized by repeated collapse of the upper airway resulting in restriction of breathing
- Frequent nocturnal awakenings
- Low oxygen levels at night
- Excessive daytime sleepiness
- Present in >20% of women over the age of 60

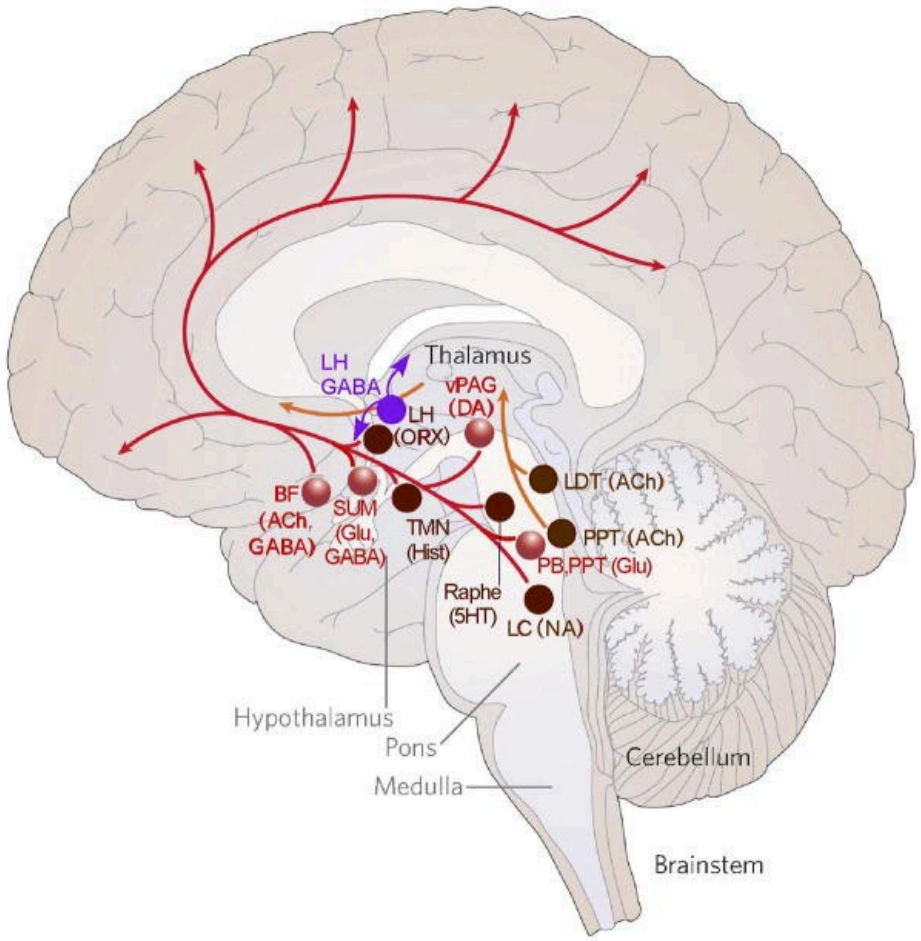


(Heinzer et al, Lancet Respir Med, 2015; n=3043 HypnoLaus Study)

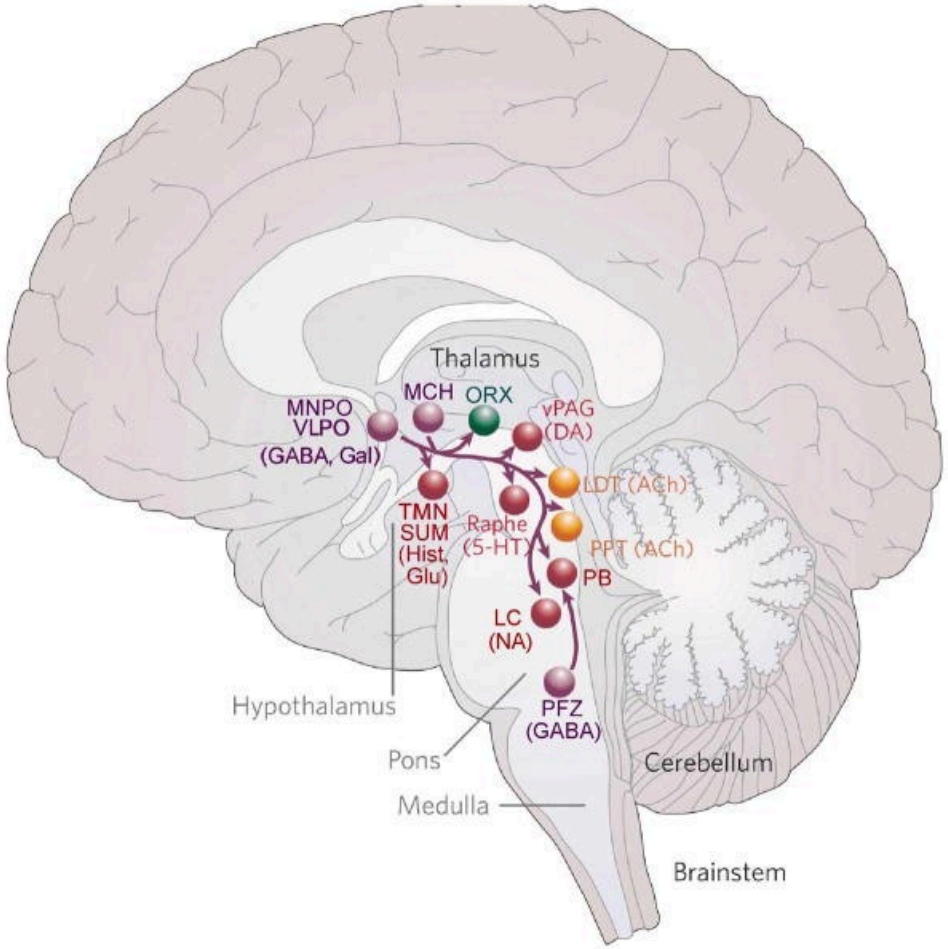
Age- and Neurodegeneration Related Damage to Sleep Regulatory Areas

The ventrolateral preoptic nucleus is the “off” switch of the brain

Wake Promoting Areas

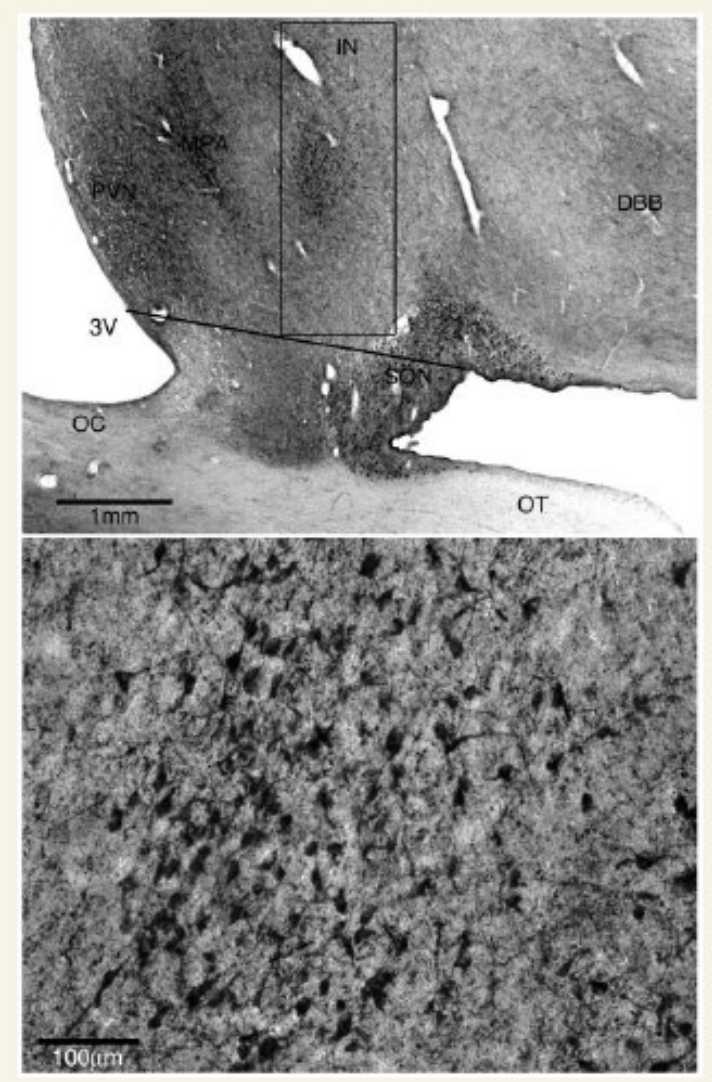


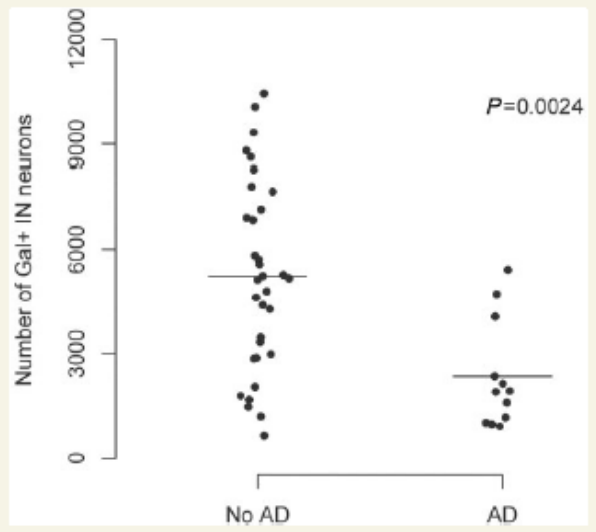
Sleep Promoting Areas

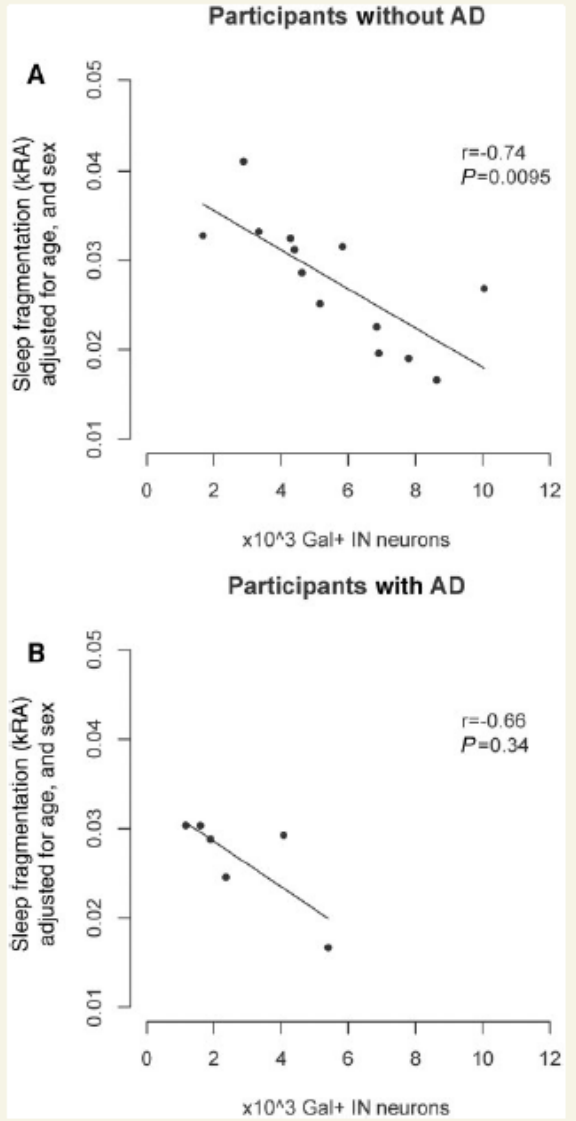


(Saper and Fuller et al, Curr Opin Neurobiol, 2017)

Neuron loss in the ventrolateral preoptic nucleus of the hypothalamus correlates with sleep fragmentation



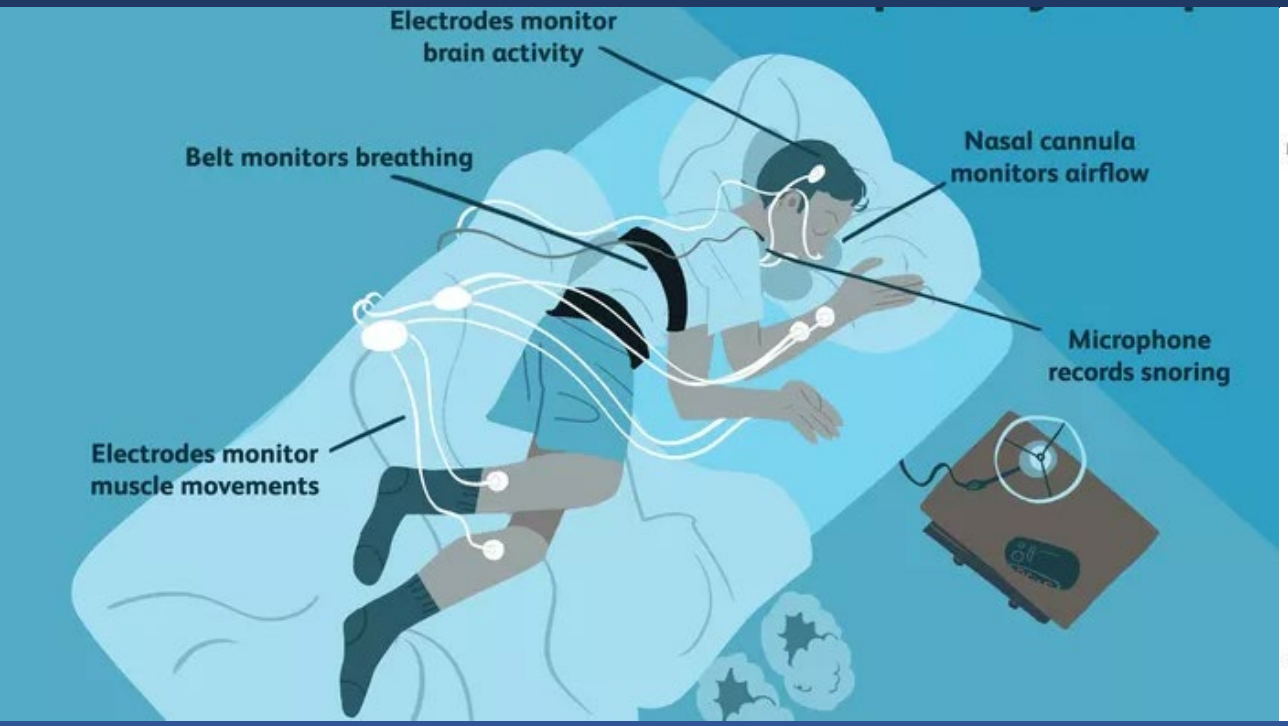


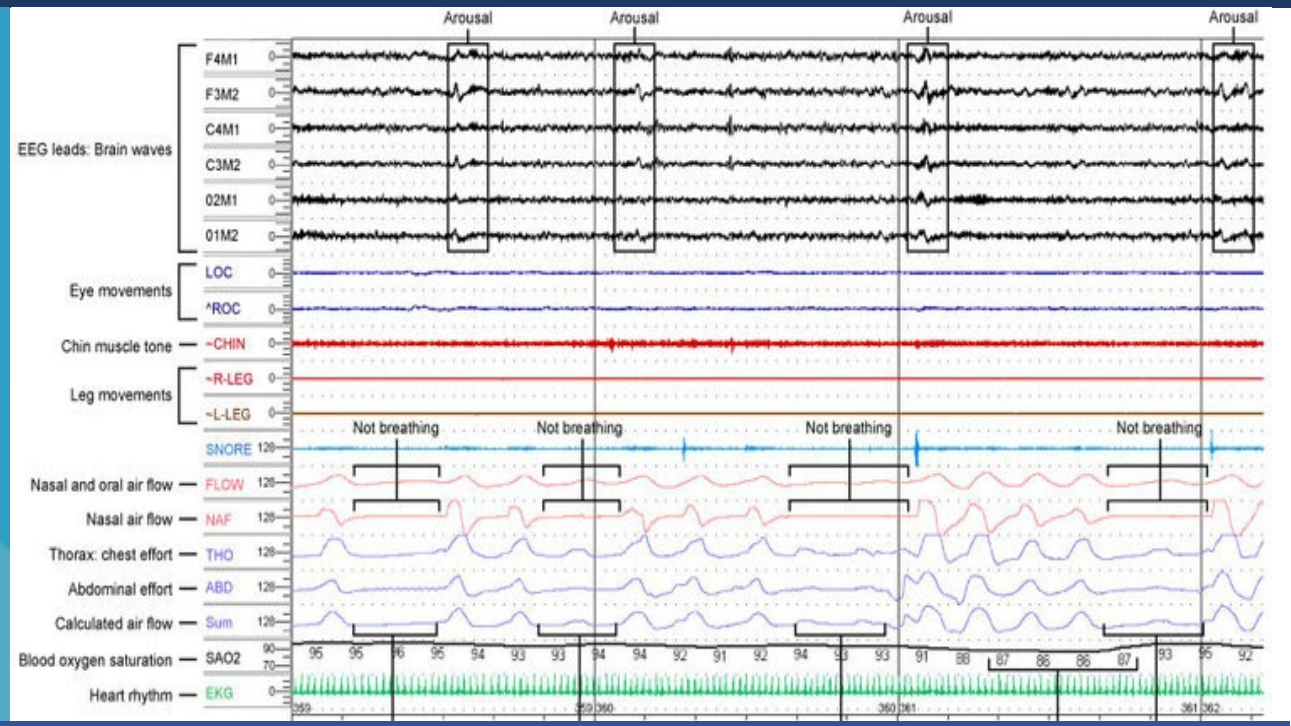


Lim et al, Brain, 2014 (n=45; 70% Female; Rush Memory and Aging Project)

How do we make a diagnosis?

Current Clinical Standard: In-Lab Sleep Study





- Uncomfortable
- Expensive
- Requires specialized technician/MD
- Cannot measure circadian rhythms – confounded by external light/sound stimuli

Coming Soon: Wearable Technologies for Sleep Measurement

MUSE Headbands

- EEG, PPG, Accelerometer

ANNE Patches

- ECG, PPG, Accelerometer

Wrist actigraphy

Geneactiv

Axivity

- Accelerometer 3D, temperature

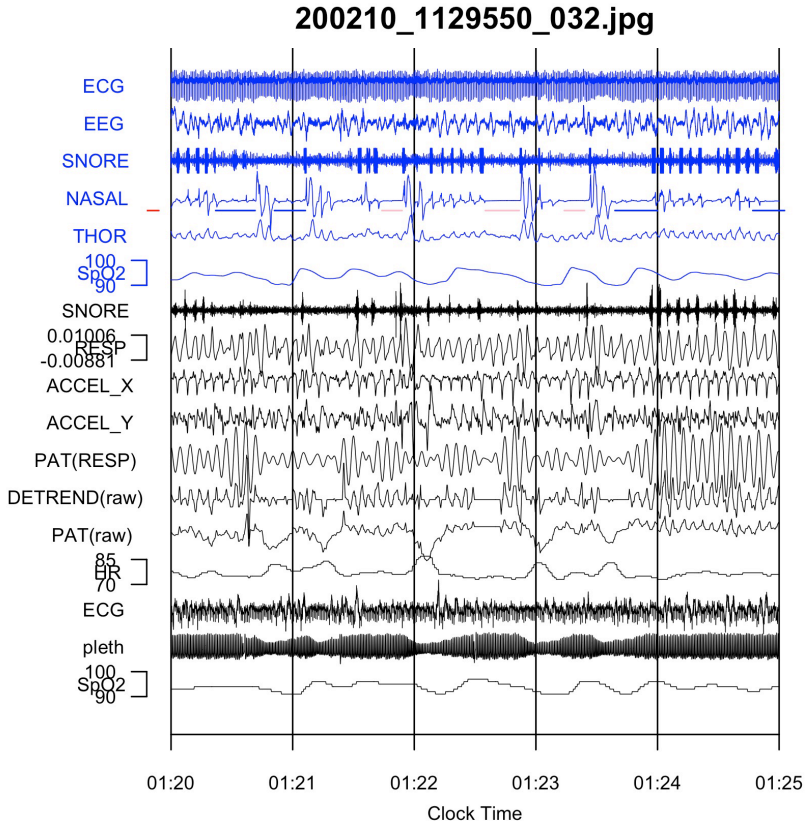
Machine Learning Algorithms

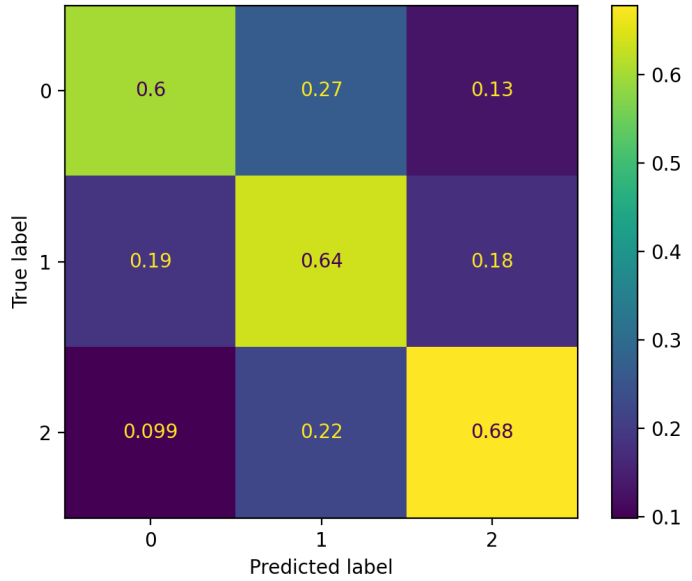
- Sleep staging

- Detecting sleep apnea
- Sleep staging

- Sleep staging
- Circadian rhythmicity

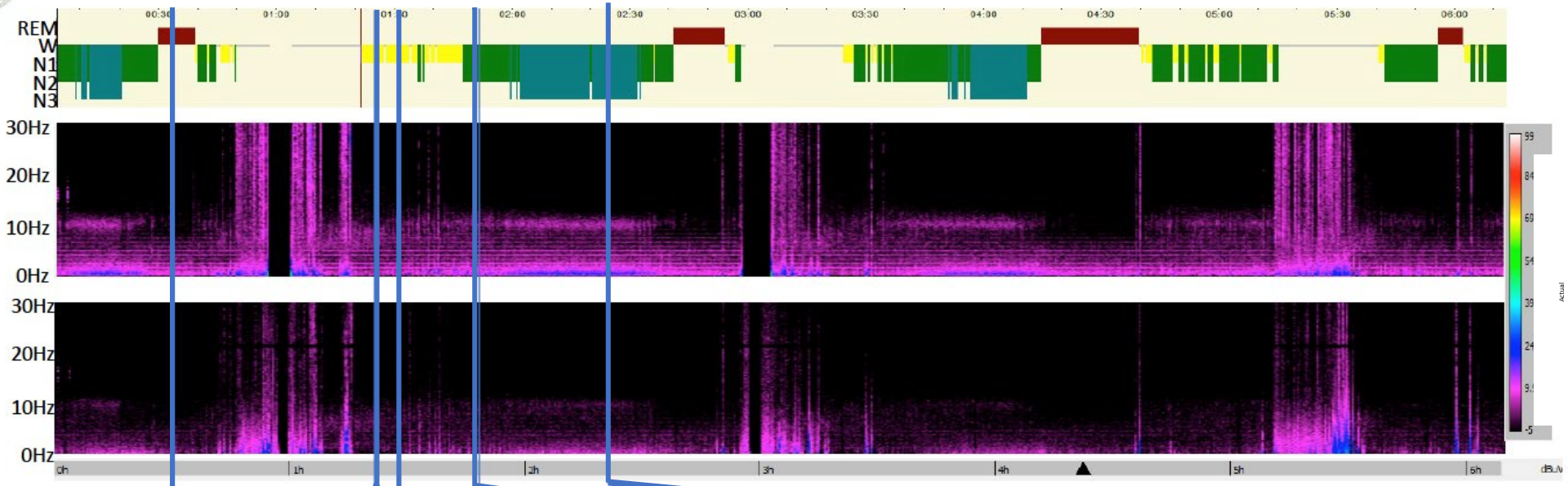
ANNE Sensors for Apneas and Sleep Staging

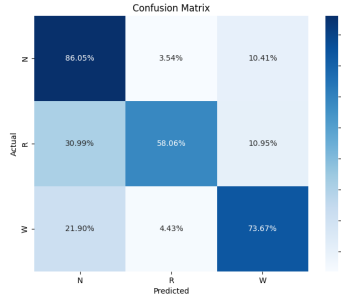




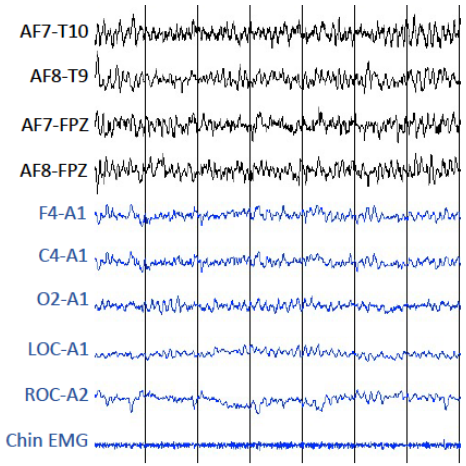
Andrew Zhang and Alex He-Mo, Unpublished

MUSE

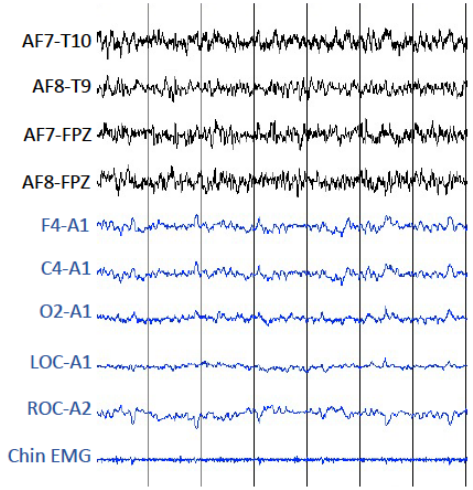




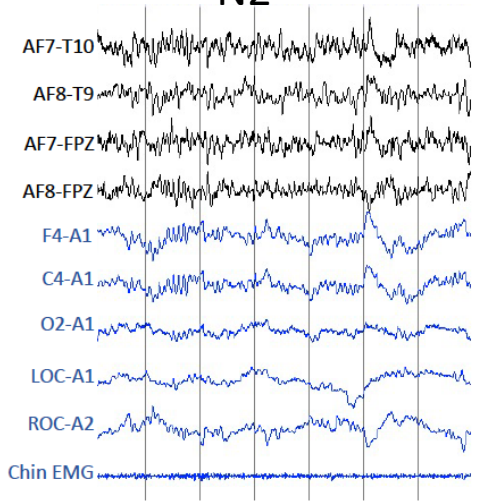
Wakefulness



N1



N2



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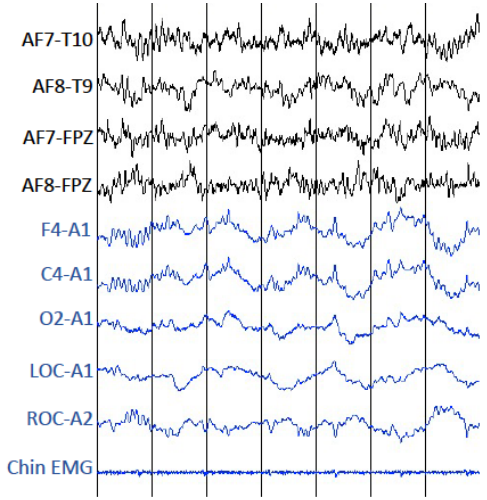
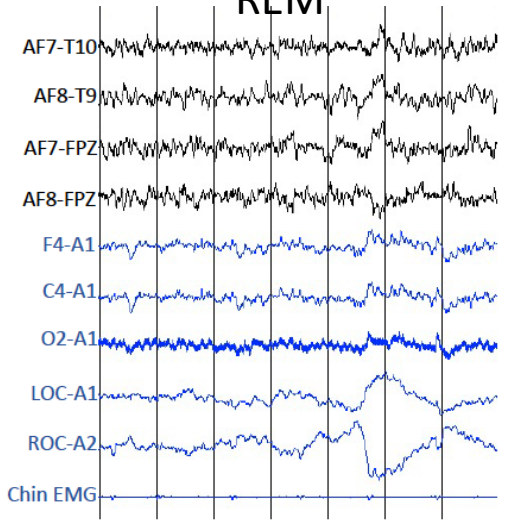


REM

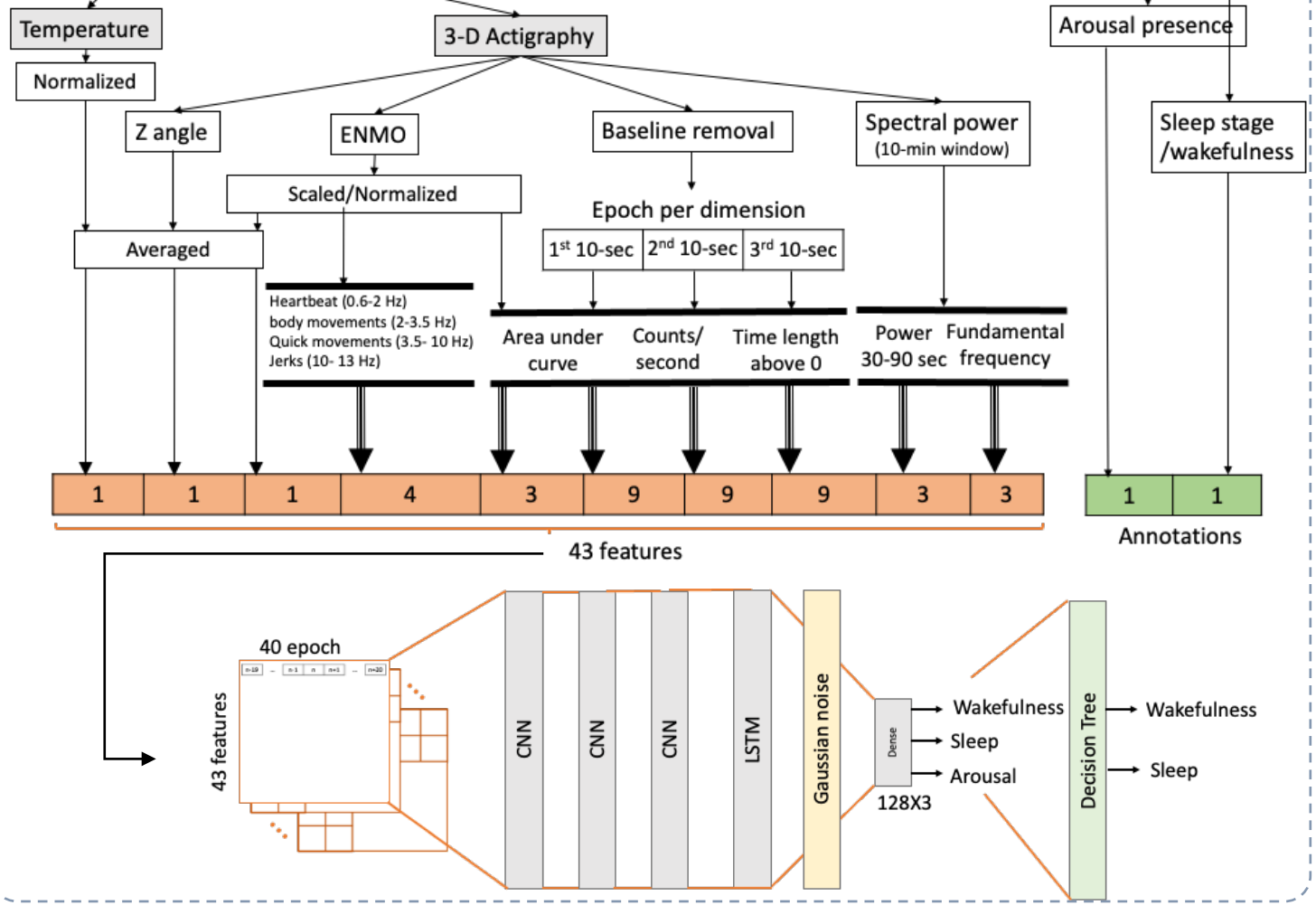


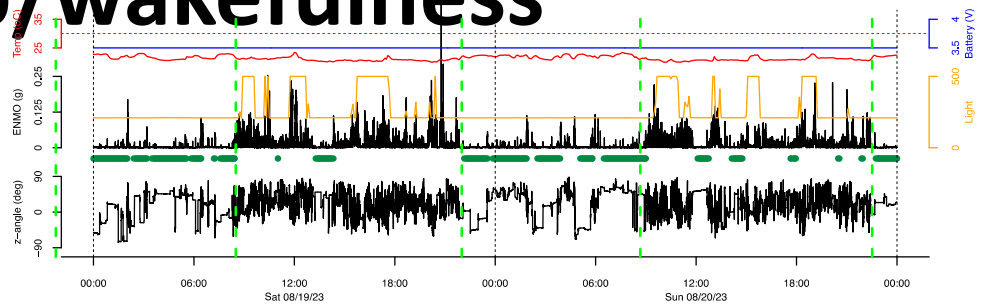
Dharmendra Gurve, Unpublished

Actigraphy to detect sleep/wakefulness

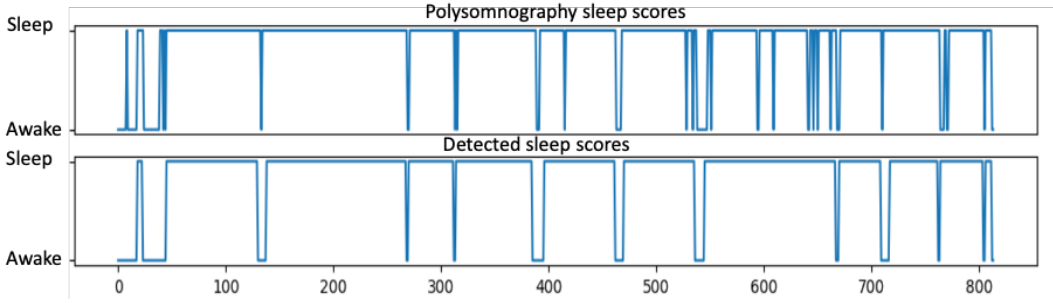
Method

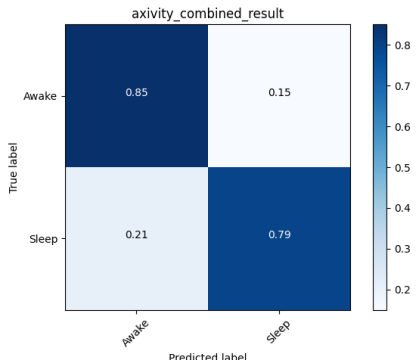
Simultaneous





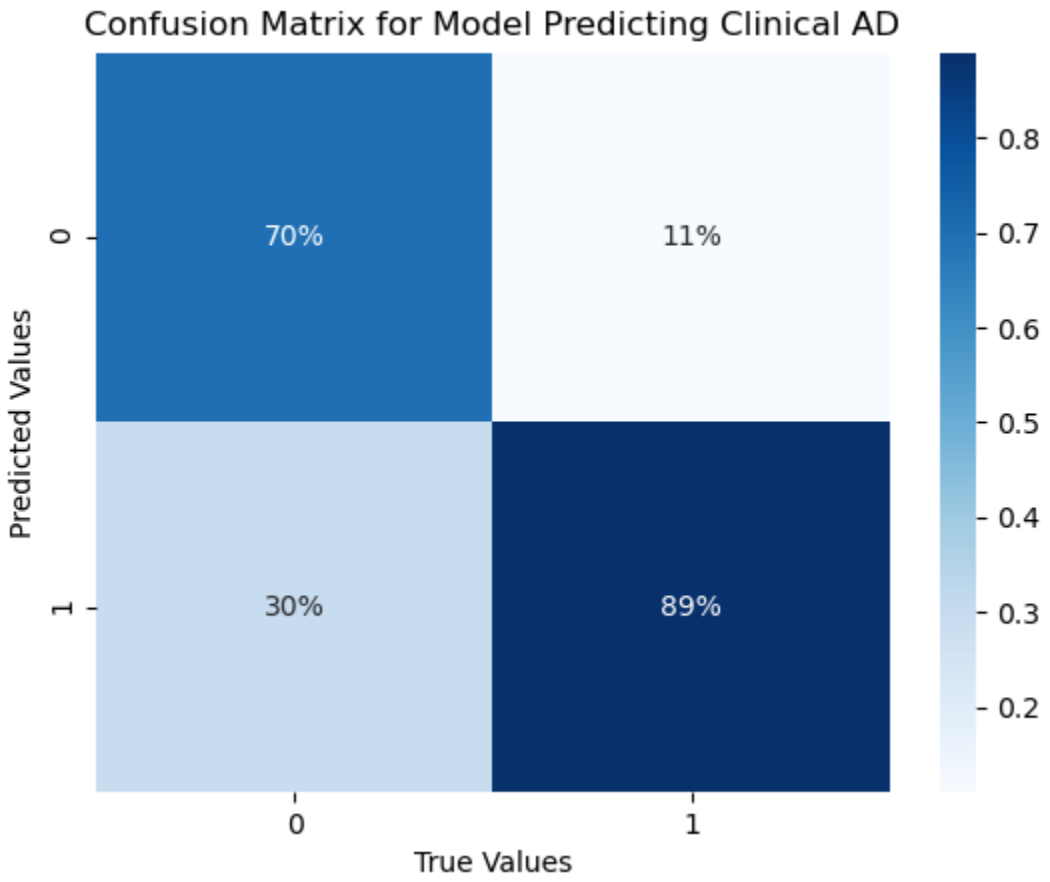
Actigraphy brand	f1	Sensitivity (Sleep)	Specificity (Awake)	Precision	Accuracy
Axivity (trained)	90.32	90.79	71.19	91.76	**85.32**
Geneactiv	84.67	97.47	68.69	84.48	**81.29**

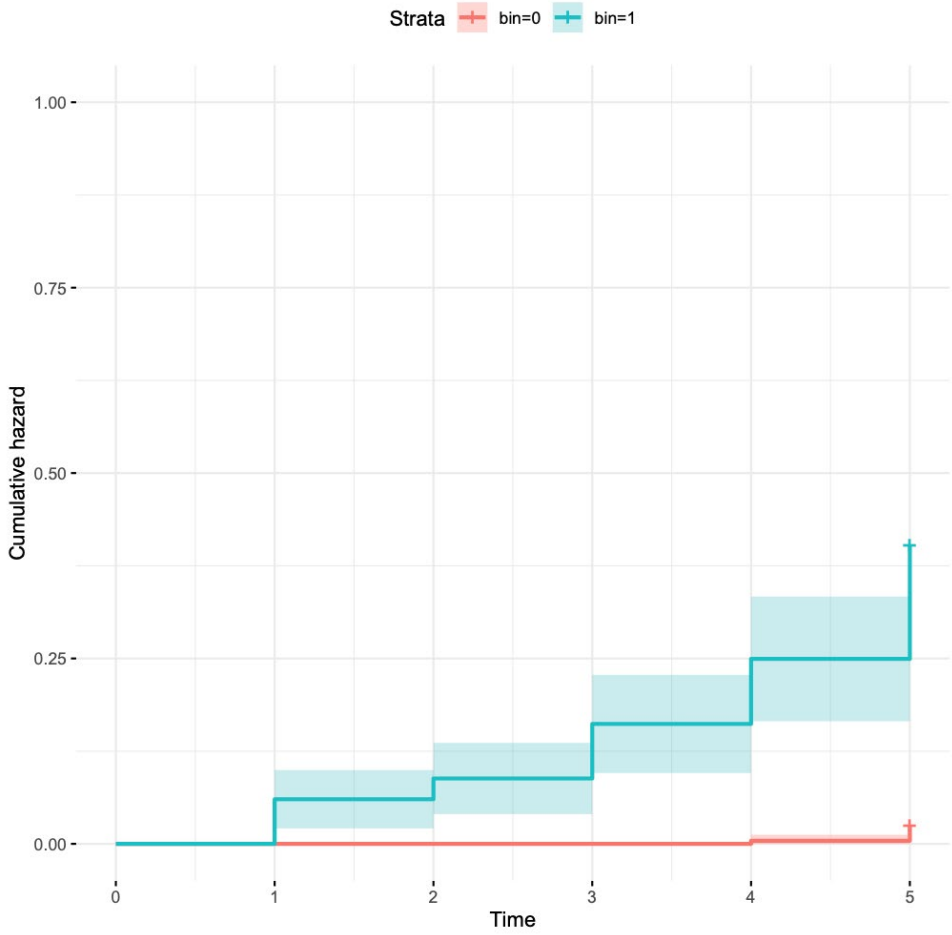




Nasim Montazeri, Unpublished

Actigraphy to Predict Dementia





Julie Midronie, Unpublished

Question 2: I’m worried about my memory difficulties. Are these at all related to my difficulties with sleep?

The Rush Memory and Aging Project

Cohort PI: Dr. David Bennett

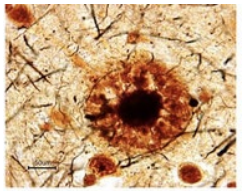
~1000 non-demented older community-dwelling adults ~72% female

Cognitive Testing
10d Actigraphy

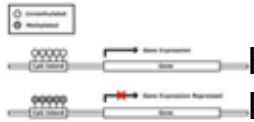
Cognitive Testing
10d Actigraphy

Cognitive Testing
10d Actigraphy

Deceased → Autopsy



Neurodegenerative pathologies



Bulk RNAseq

Fragmented Sleep is Associated with Risk of Alzheimer's

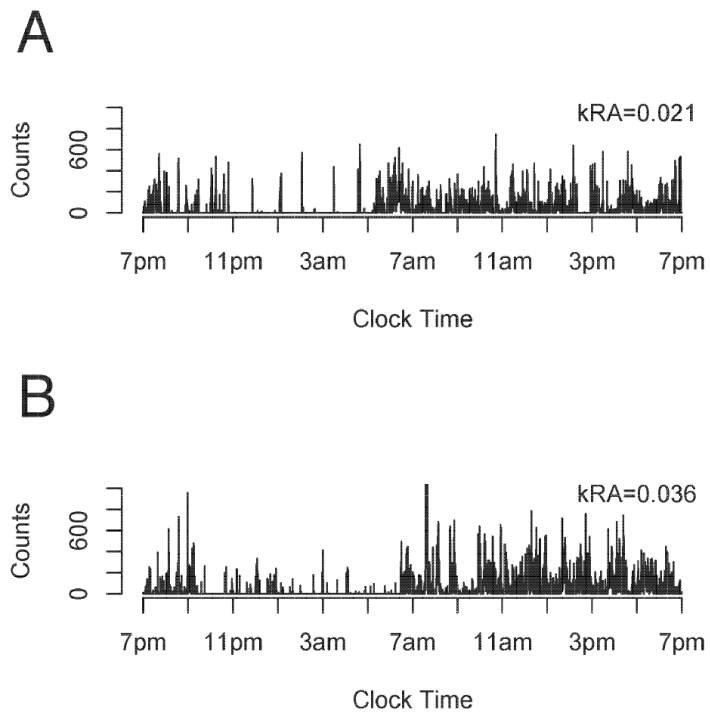


Figure 1—Illustrative actigraphic recordings. 24 h of actigraphy from two representative participants at the 10th (Panel A; k_{RA} 0.021) and 90th (Panel B; k_{RA} 0.036) percentiles of sleep fragmentation.

Incident Alzheimer's Disease

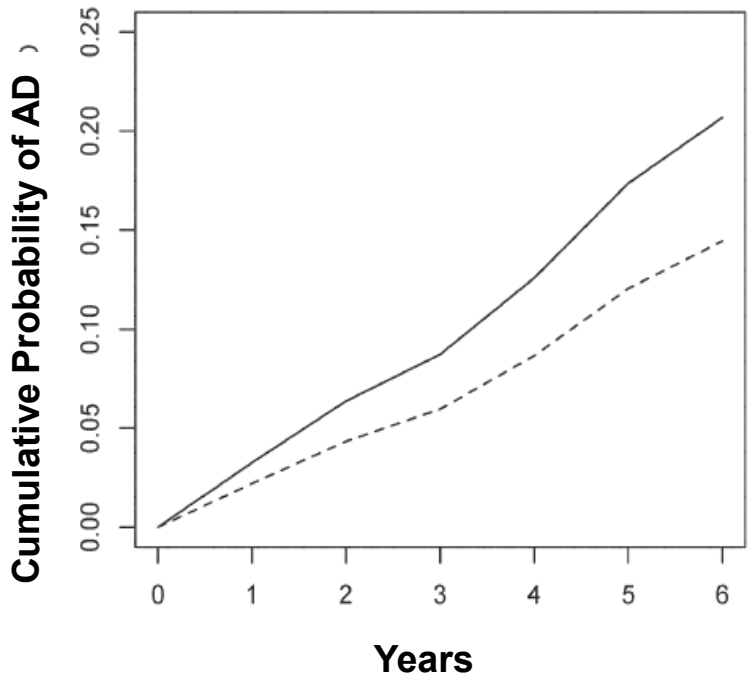


Figure 2—Expected risk of AD. The model predicted risk of AD based on the entire cohort is illustrated for two hypothetical average participants with high (Solid line: 90th percentile; k_{RA} = 0.036) and low (Dotted line: 10th percentile; k_{RA} = 0.021) levels of sleep fragmentation.

Cognitive Decline

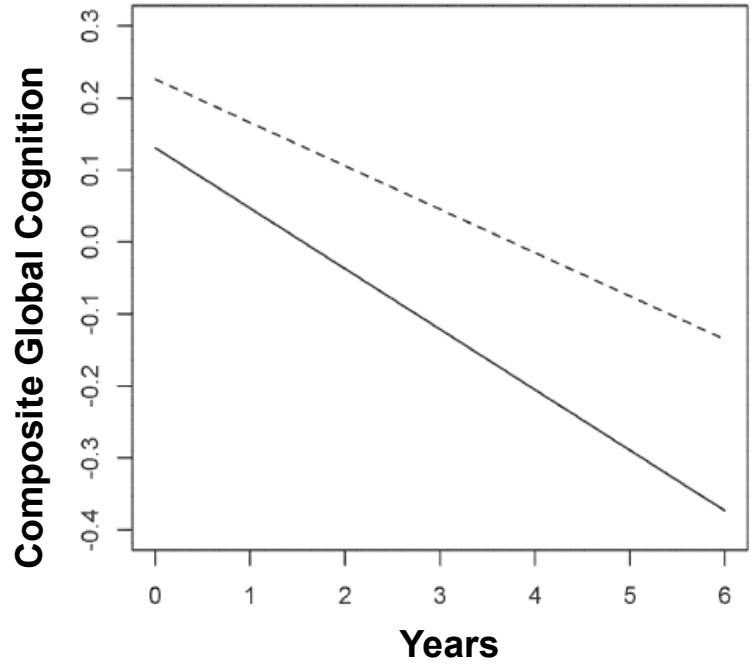


Figure 3—Expected cognitive decline. The model predicted rate of global cognitive decline based on the entire cohort is illustrated for 2 hypothetical average participants with high (Solid line: 90th percentile; k_{RA} = 0.036) and low (Dotted line: 10th percentile; k_{RA} = 0.021) levels of sleep fragmentation.

Lim et al, Sleep, 2013 (n=737; Rush Memory and Aging Project)

What are the mechanisms?

The Rush Memory and Aging Project

Cohort PI: Dr. David Bennett

~1000 non-demented older community-dwelling adults ~72% female

Cognitive Testing
10d Actigraphy

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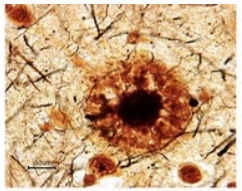
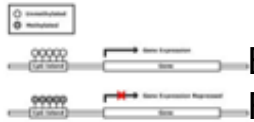
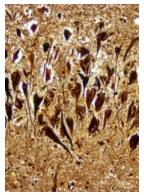


Neurodegenerative pathologies

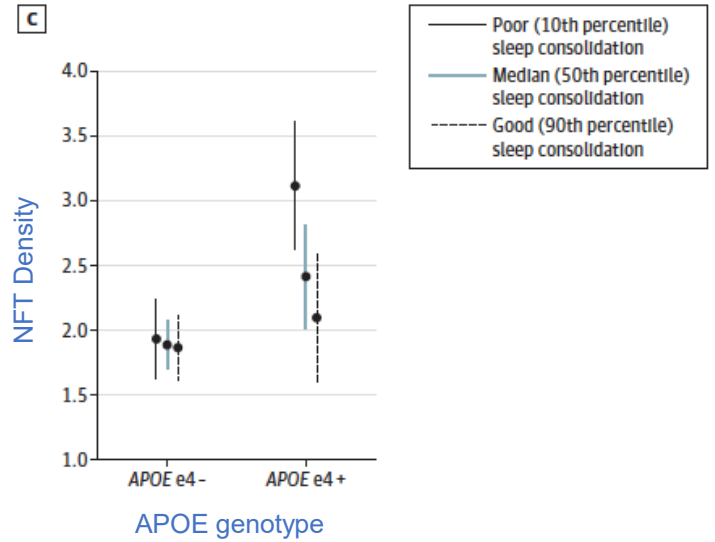


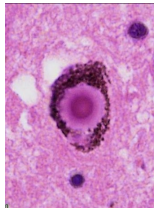
Bulk RNAseq

Individuals with Sleep Disruption have a Higher Burden of Multiple Dementia Pathologies

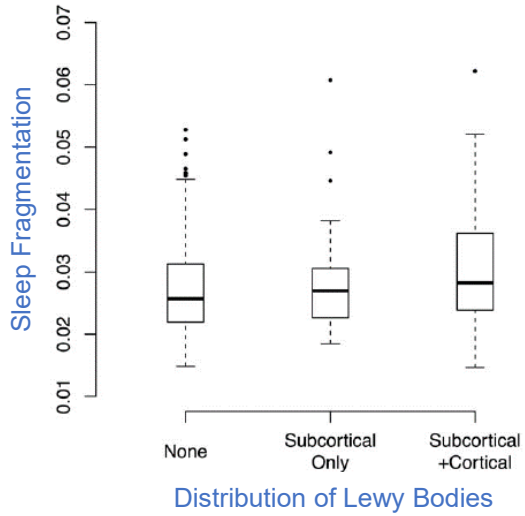


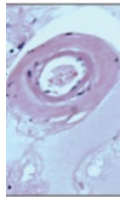
Neurofibrillary Tangles[1]



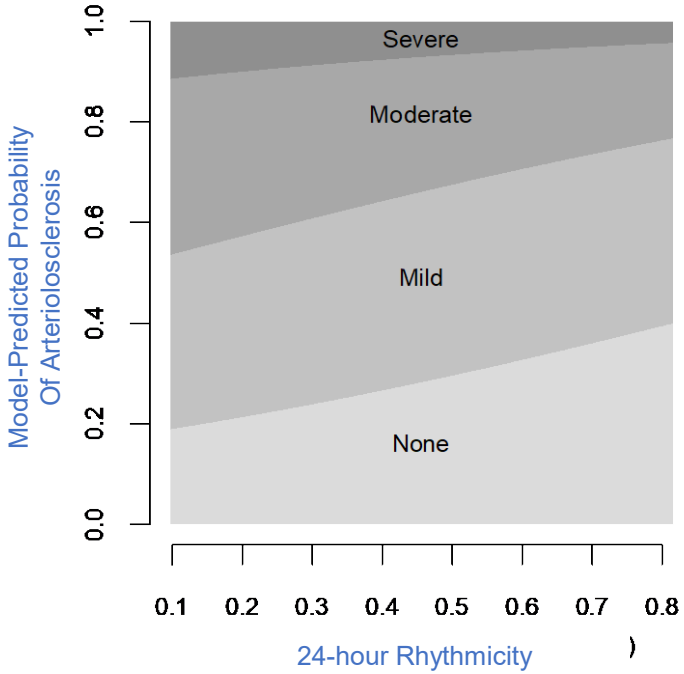


Lewy Bodies[2]





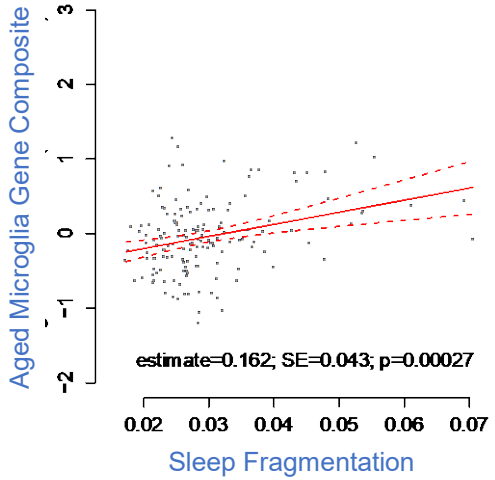
Arteriolo-Sclerosis[3,4]

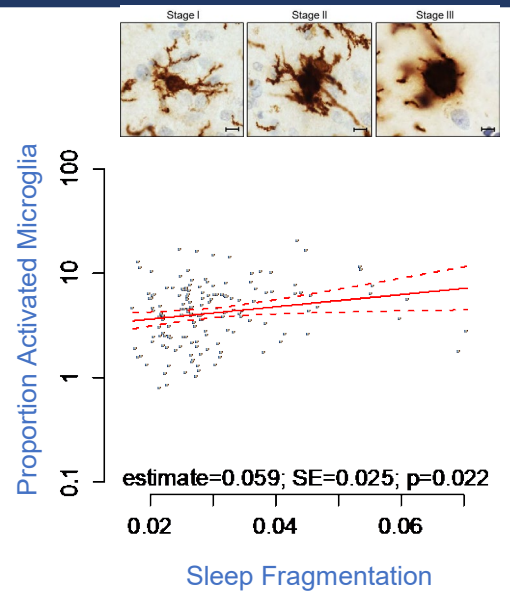


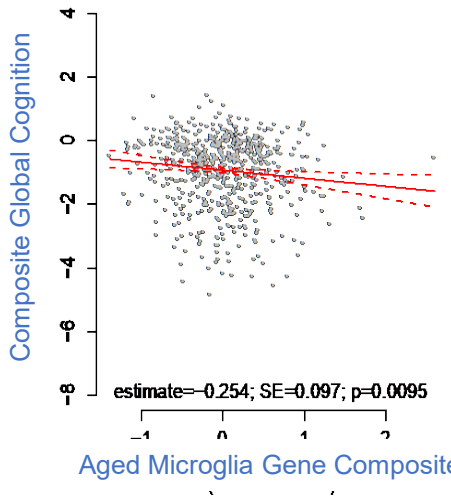
1. Lim et al, JAMA Neurol, 2014
2. Sohail et al, Mov Disord, 2017
3. Lim et al, Stroke, 2016
4. Sommer et al, Stroke, 2021

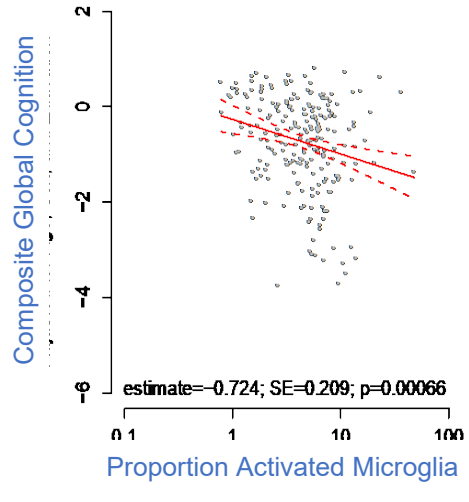
Individuals with Sleep Disruption Have Greater Microglial and Astrocyte Activation

Microglia[1]

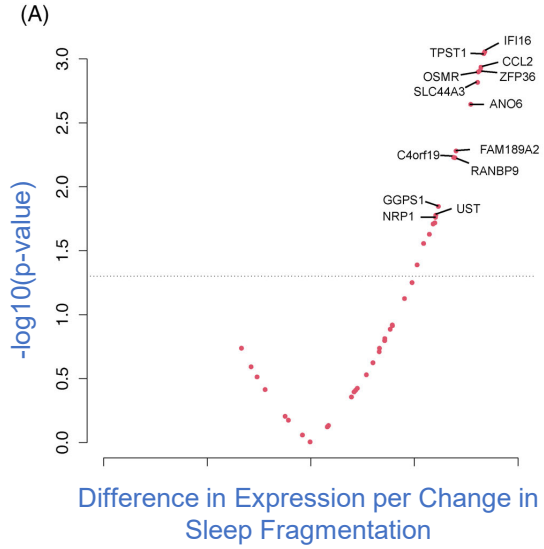


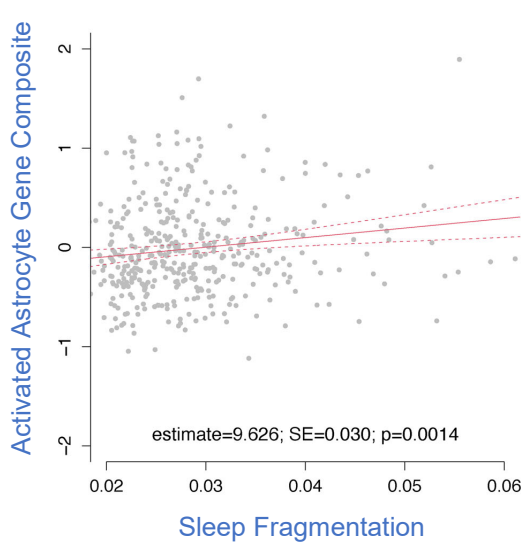


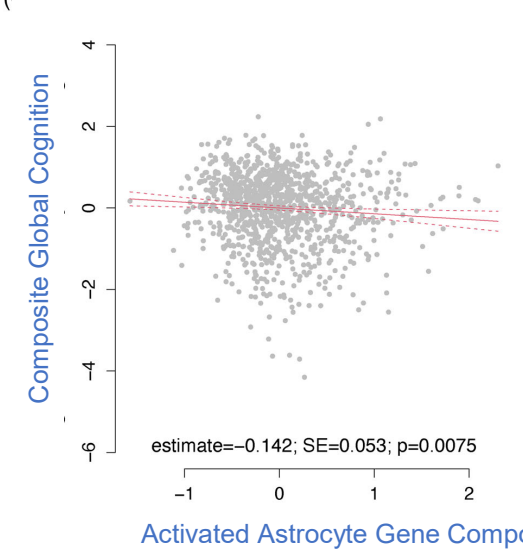


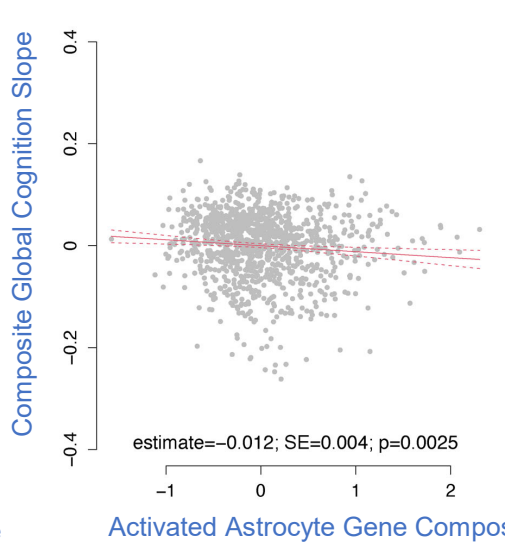


Astrocytes[2]



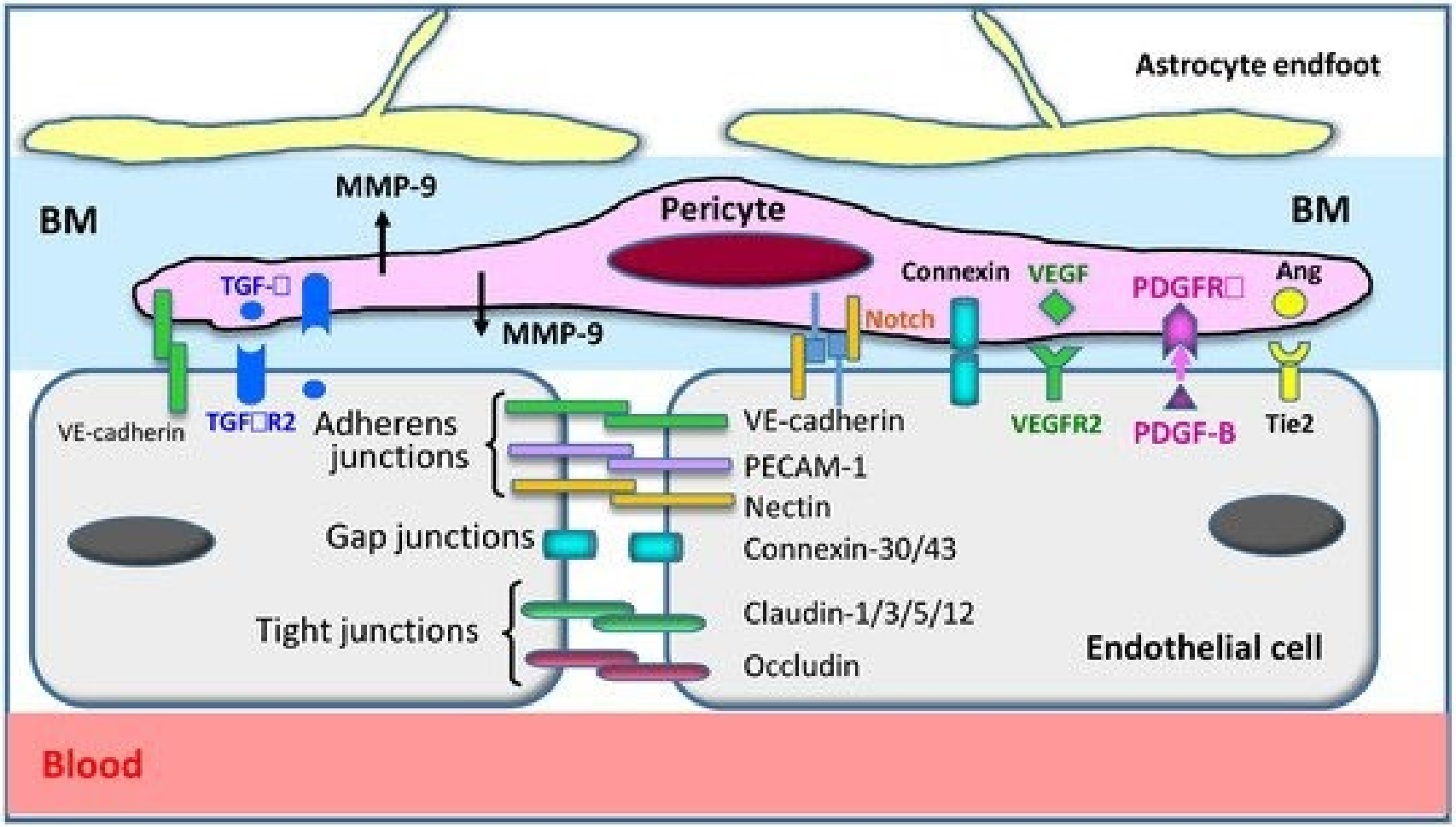






1 Kaneshwaran et al, Science Advances, 2019)
2 Wu et al, Alzheimers Dement, 2022)

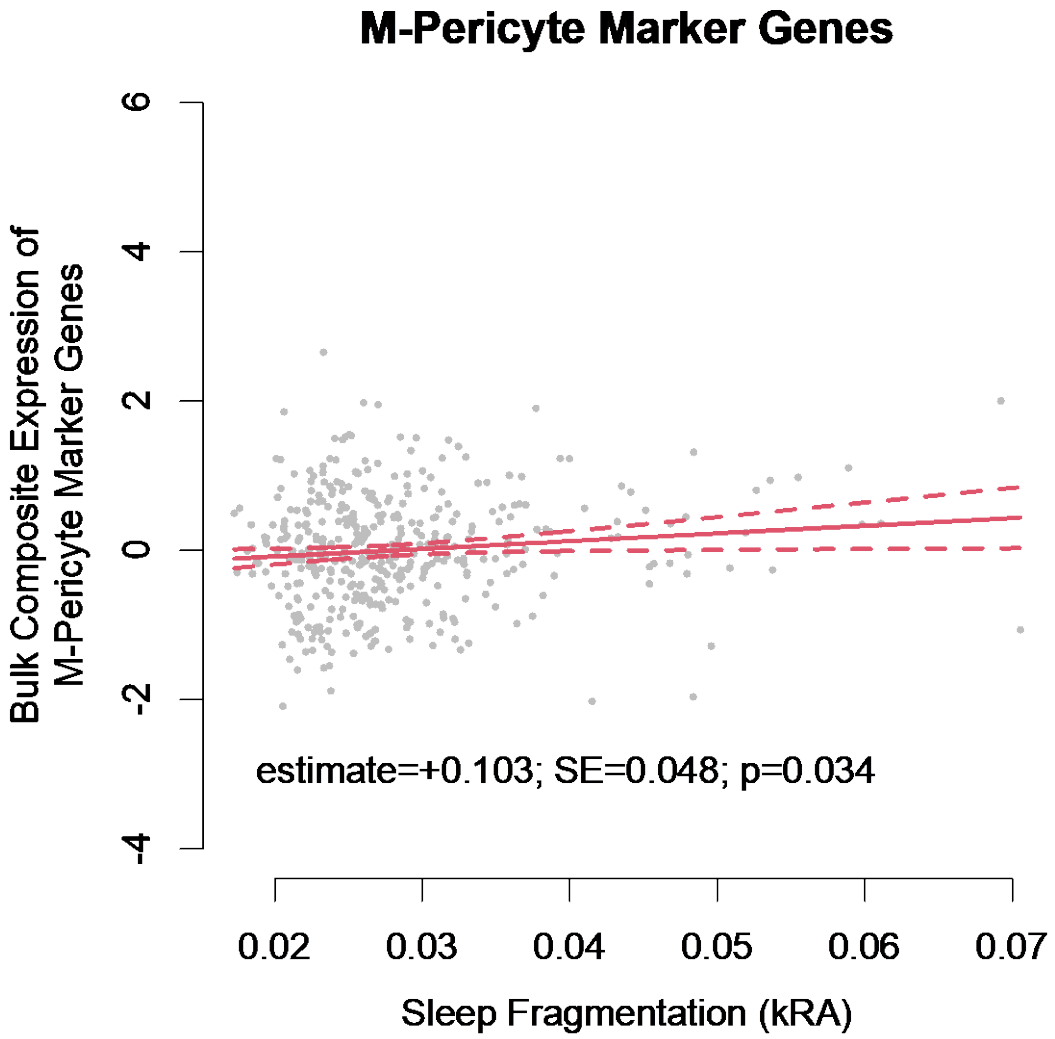
Individuals with Sleep Disruption Have a Shift Toward M-type Pericytes



- Blood-Brain Barrier
- Neurovascular coupling
- Angiogenesis

(Nishibori et al, Cells, 2020)

Individuals with Sleep Disruption Have a Shift Toward M-type Pericytes



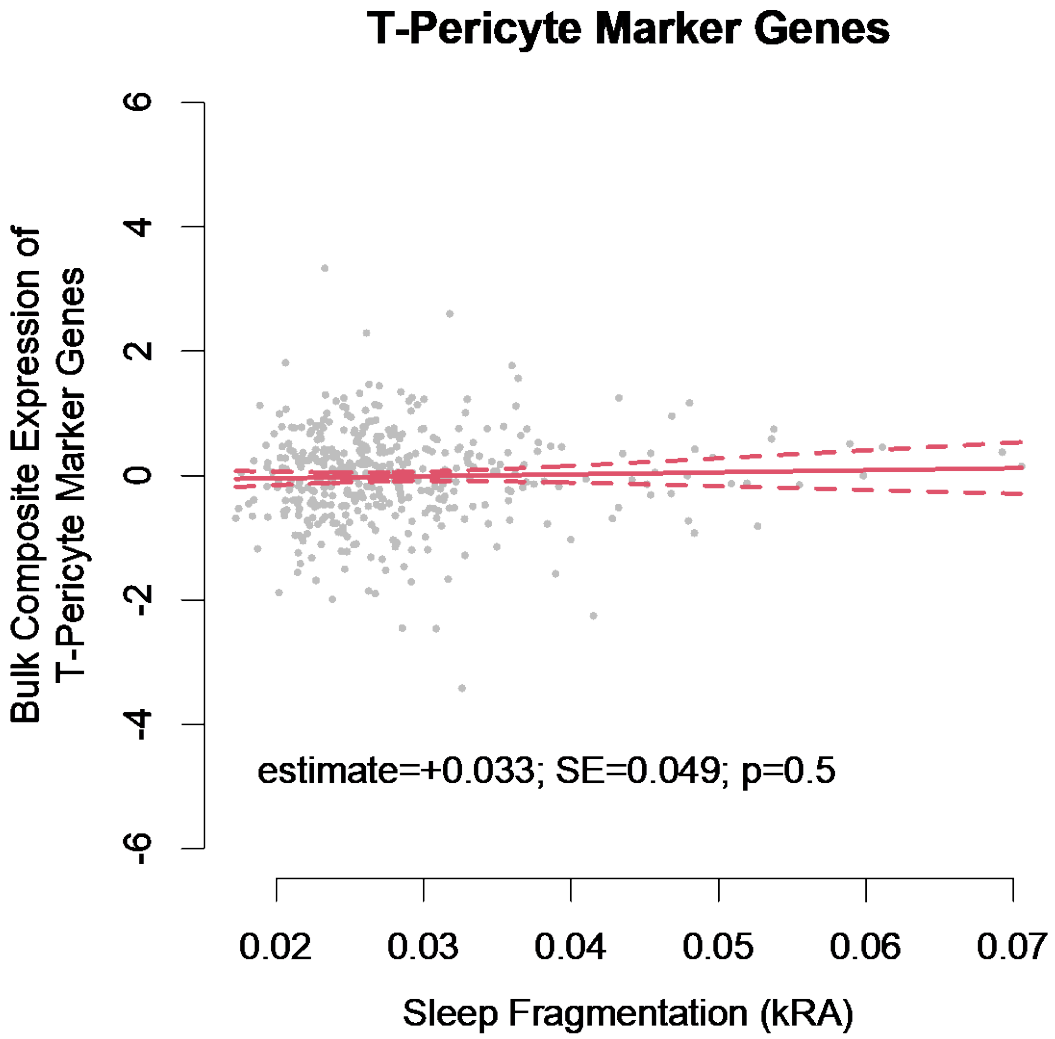


Figure 5: Composite expression of M- and T- pericyte marker genes as a function of average antemortem sleep fragmentation.

Hamid et al, World Sleep Congress, 2023

Individuals with Sleep Disruption Have a Shift Toward M-type Pericytes

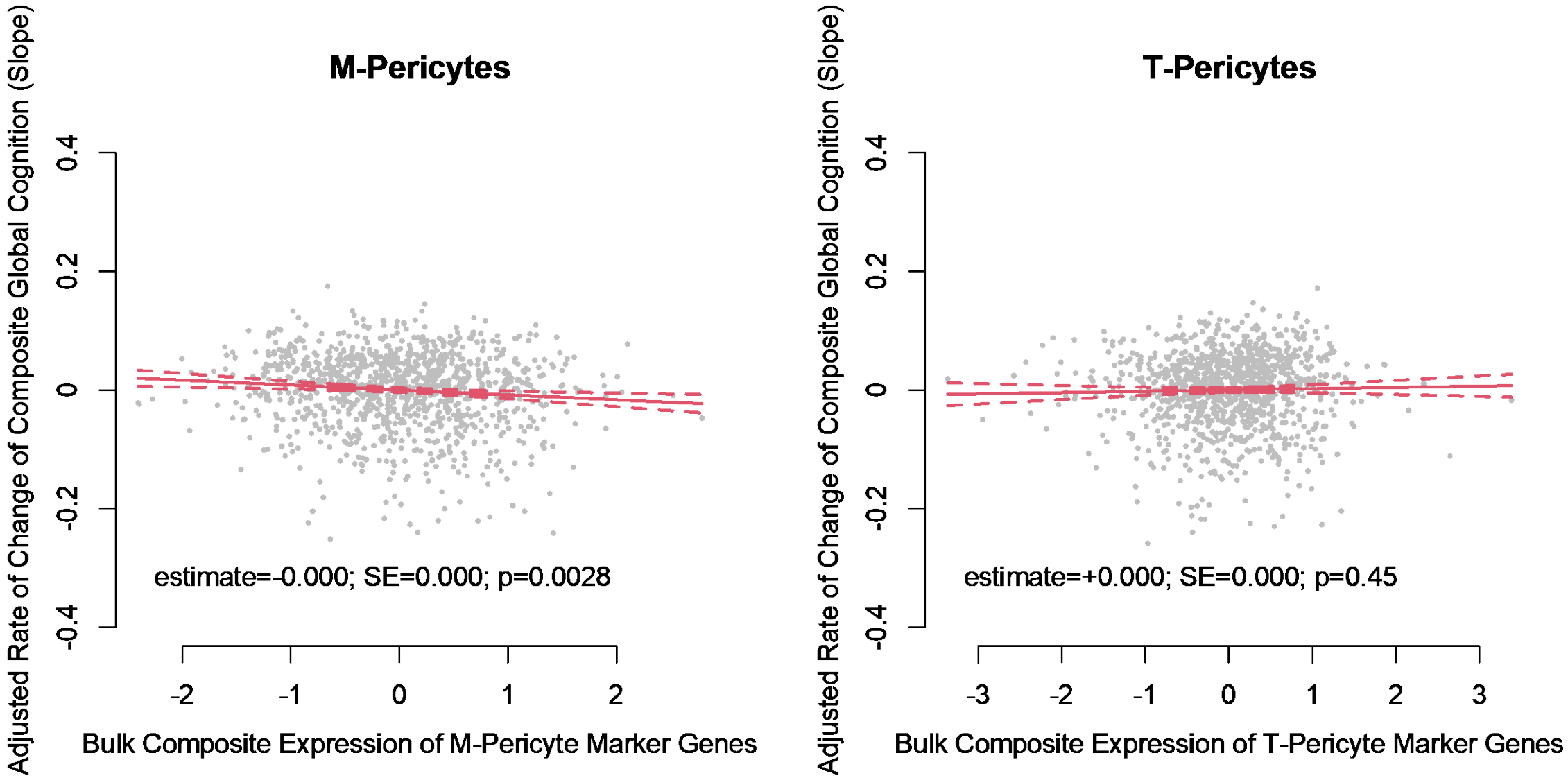


Figure 6: Rate of change of composite global cognition as a function of M- and T- pericyte marker gene composite expression

Hamid et al, World Sleep Congress, 2023

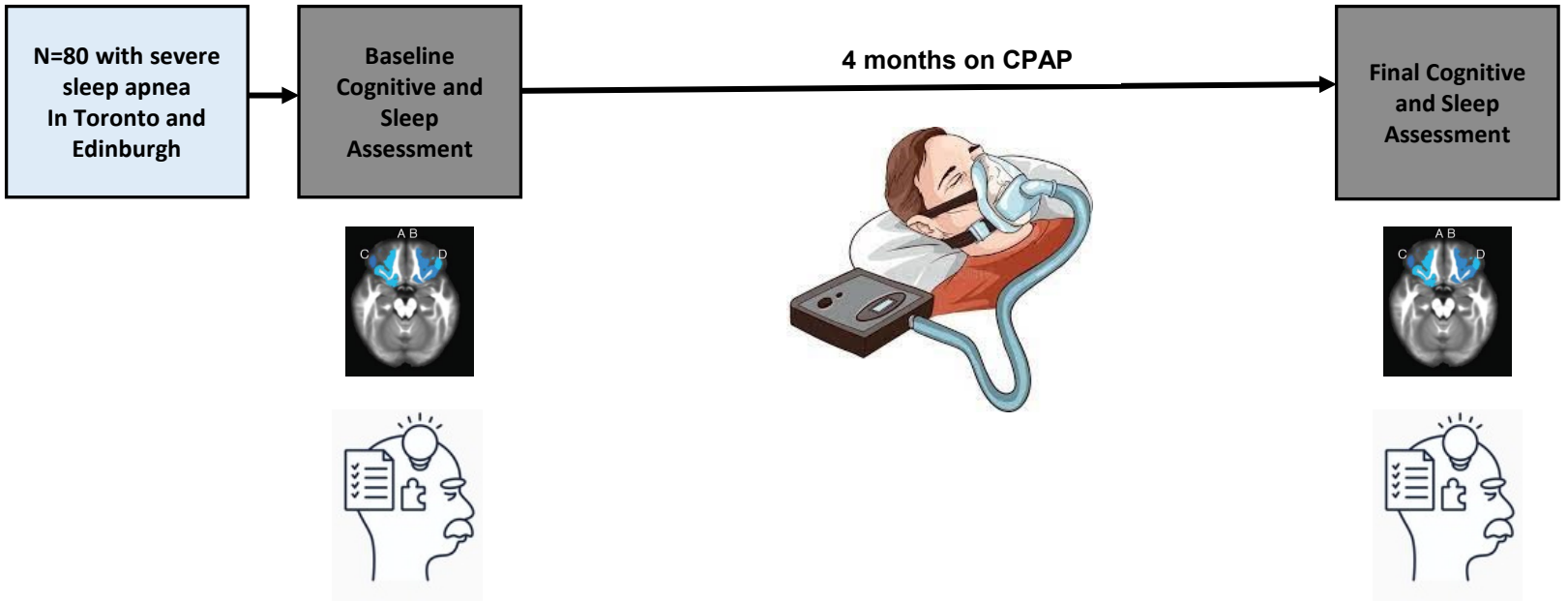
Question 3: What can I do to improve my sleep? Will improving my sleep help my memory and prevent dementia?

Insomnia and Circadian Rhythm Dysfunction – Dr. Dang-Vu

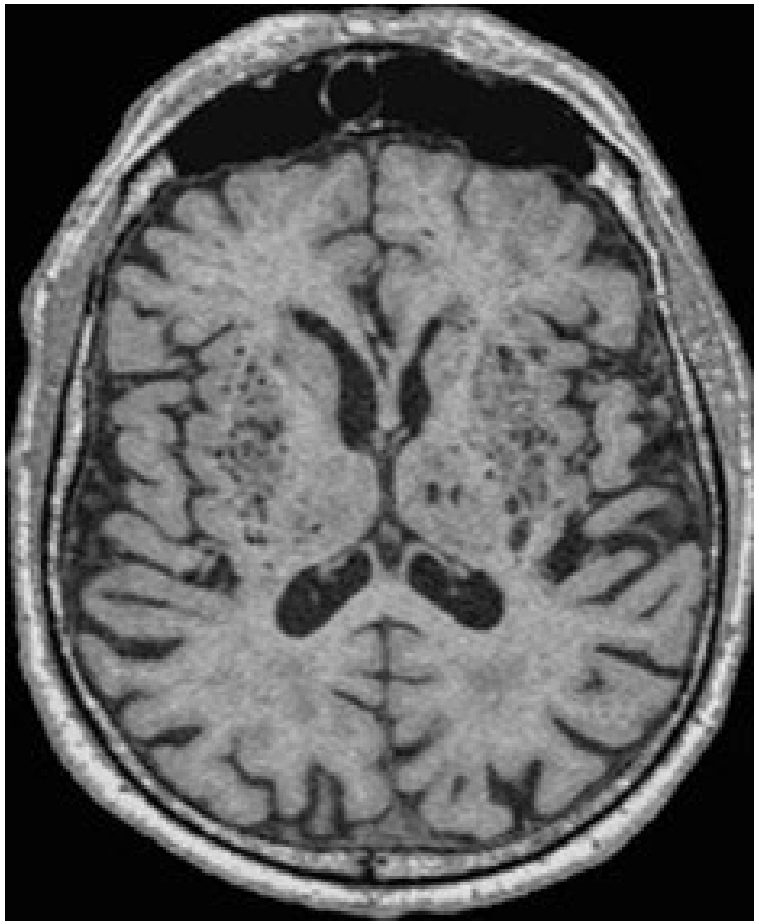
Sleep Apnea

The Brain Changes in Sleep Apnea Study

Question: Does CPAP improve cognition, brain blood flow, and brain small vessel damage in adults with sleep apnea?



Enlarged Perivascular Spaces are Correlated with Cognitive Impairment



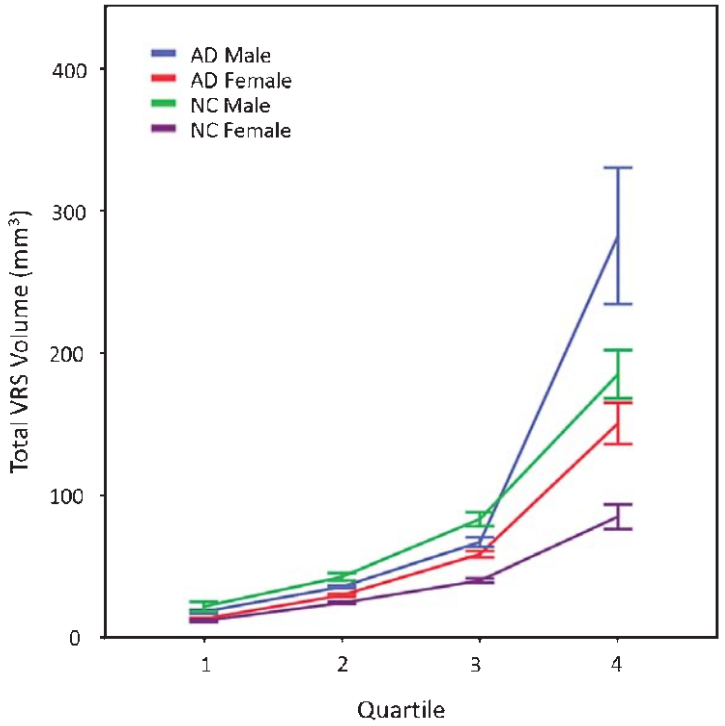
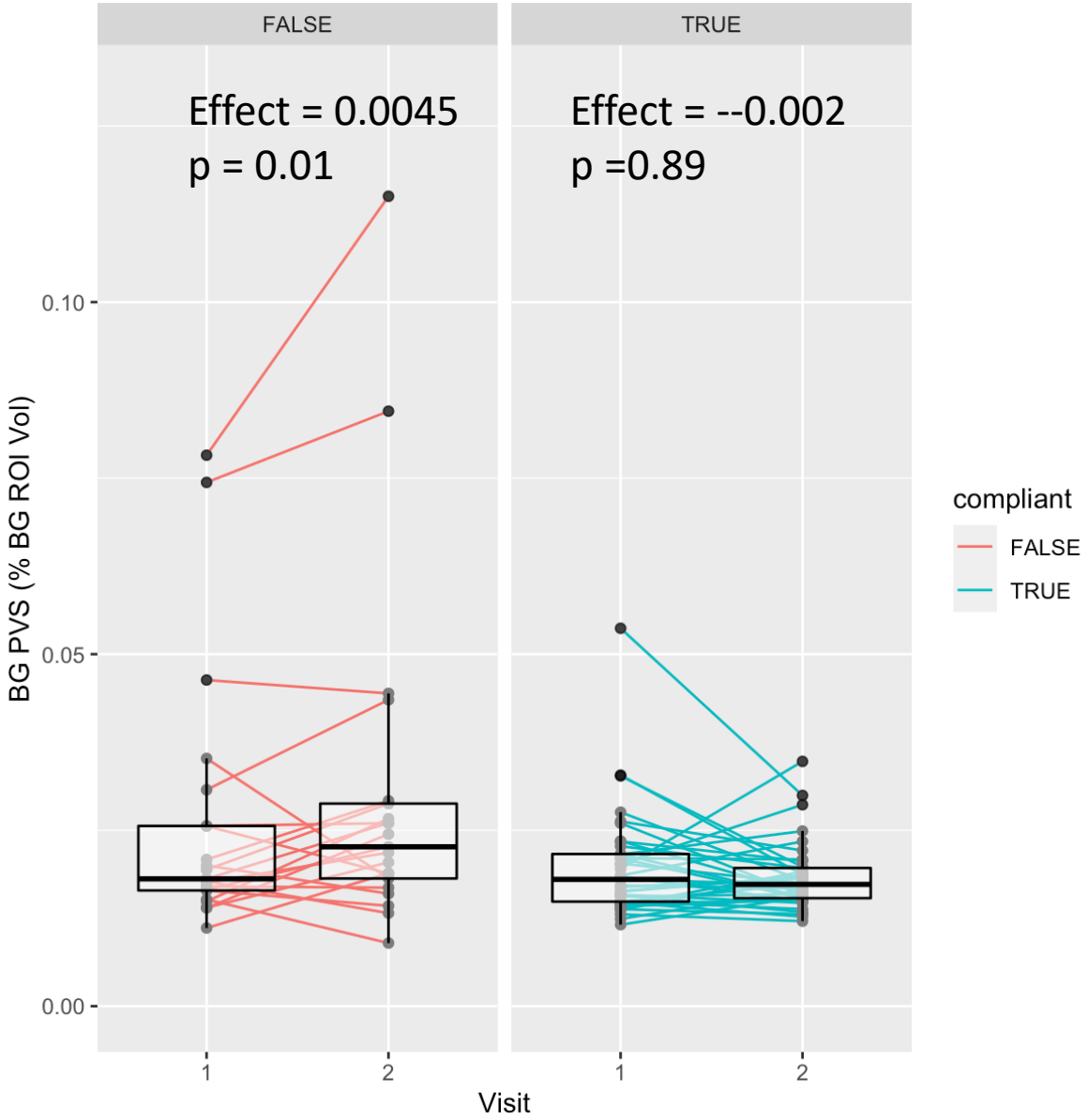


Fig. 4. VRS mean volumes in the Alzheimer's disease patients and normal elderly controls grouped by gender and quartiles (AD Male = blue, AD Female = red, NC Male = green, NC Female = purple). Error Bars represent ± 1 SE.

Ramirez et al, J Alzheimer's Dis, 2015

BG PVS volumes changes depend on CPAP compliance

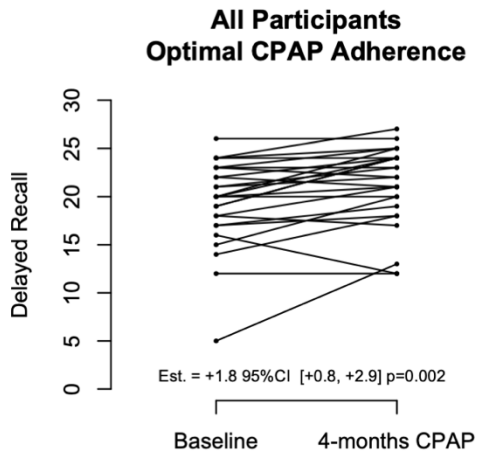


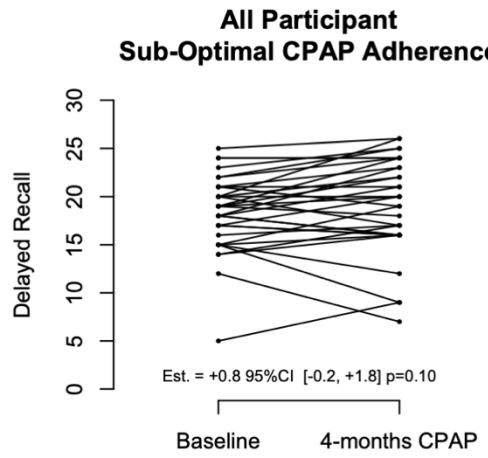
Linear Mixed Effect Model:
Sqrt(BG PVS) ~ Visit:Compliant + Age + Sex
Random: ~1|site/ID
N = 62; 70% male

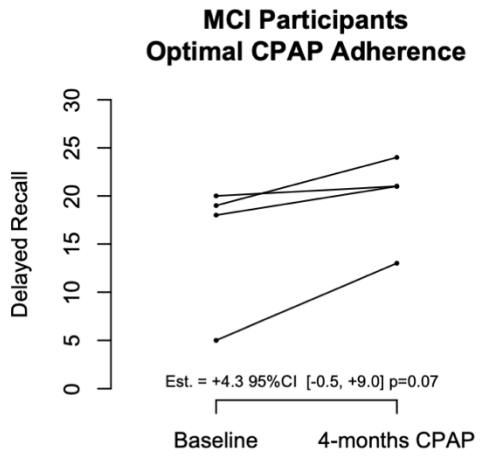
	Effect	SE	p
visit:compliant FALSE	0.0045	0.0017	0.01
visit : compliant TRUE	-0.0002	0.0014	0.89
Age	0.0004	0.0002	0.03
Sex	0.0043	0.0036	0.24

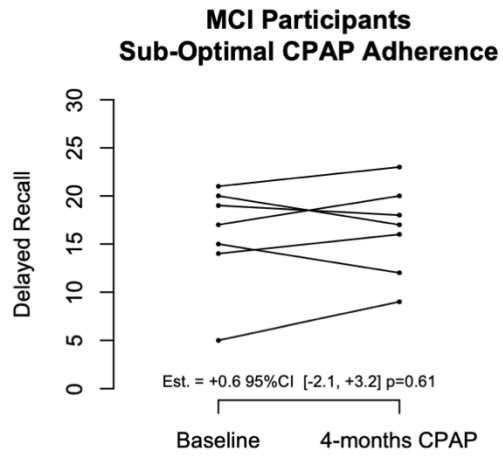
Sommer et al, Unpublished

CPAP improves delayed recall









Sommer et al, Unpublished

The Future

Beatrice’s story – in 2026

- At age 71, when she is still cognitively well, Beatrice sees her family doctor for sleep difficulties
- He gives her a soft cloth headband to wear at night, and some stickers to place on her chest and finger, along with a wristwatch to wear for a couple of weeks
- These are analyzed automatically using machine learning algorithms which suggest that
    1. Beatrice has advanced sleep phase syndrome and sleep apnea
    2. Beatrice has changes in her sleep wake pattern that suggest a higher than average risk of developing dementia in the future
- Beatrice is prescribed a wearables-guided phototherapy regimen for her circadian rhythm disorder and CPAP for her sleep apnea
- Her sleep much improved, Beatrice lives for many more years, as cognitively sharp as always

The Sunnybrook Sleep and Brain Health Lab

Current Members

Andrew Centen, MSc
Dharmendra Guru, PhD
Erin Gibson, PhD
Trishan Saha-Detroja, PhD
Rosa Sommer
Mahnoor Hamid
Aishwaria Maxwell
Julie Midroni
Andrew Zhang
Lokeesan Kaneshwaran
Alex He-Mo
Ricky Cheuk
Zhao Ji Wang
Arabi Guruparan
Ayan Hassan
Shreya Shridhar
Jeevetha Nesabaskaran

Recent Alumni

Nasim Montazeri
Rebecca Wu
Kirusanthy Kaneshwaran
Shahmir Sohail

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Sandra Black, Sunnybrook
Brad McIntosh, Sunnybrook
Joel Ramirez, Sunnybrook
Joanna Wardlaw, Edinburgh
Lizzie Hill, Edinburgh
Philip De Jager, Columbia
David Bennett, Rush U
Aron Buchman, Rush U
Julie Schneider, Rush U
Lei Yu, Rush U
Thanh Dang-Vu, Concordia
Howard Chertkow, Baycrest
Manuel Montero-Odasso, UWO

CENTRE FOR AGING + BRAIN HEALTH INNOVATION
Powered by Baycrest

NIH National Institutes of Health

Fondation Leducq

CIHR IRSC

Sleep and cognitive decline:
from mechanisms to interventions

Insomnia disorder :
Cognitive impact and management

- **Thanh Dang-Vu, MD PhD FAASM**
- Neurologist, Associate Director for Clinical Research, Institut universitaire de gériatrie de Montréal
- Professor, Concordia University
- Vice-President (Research), Canadian Sleep Society

- **February 13th 2024**

Conflicts of interest

Name of the company	Affiliation Type	Date
Eisai	Consultant Speaker	2019-2024
Idorsia	Consultant	2023-2024
Paladin Labs	Consultant Grant funding	2021-2022
Jazz Pharmaceuticals	Consultant Speaker Grant funding	2021-2023

Insomnia : definition and impact

~ 13%

Canadians fulfil criteria for insomnia disorder

Criteria for insomnia disorder

I. Difficulties intiating and/or maintaining sleep **despite appropriate sleep environment**

II. **At least 3 times per week**, for **at least 3 months**

III. Leads to significant distress and **disruption of daytime function**

[†]Morin, C. M. 2020.The burden of insomnia disorders. Canadian Journal of Diagnosis (Vol 38 No.3)

[‡] DSM-IV to DSM-5 Insomnia Disorder Comparison - Impact of the DSM-IV to DSM-5 Changes on the National Survey on Drug Use and Health - https://www.ncbi.nlm.nih.gov/books/NBK519704/table/ch3.t36/

Insomnia : definition and impact

~ 13%

Canadians fulfil criteria for insomnia disorder

III. Affects daytime functioning

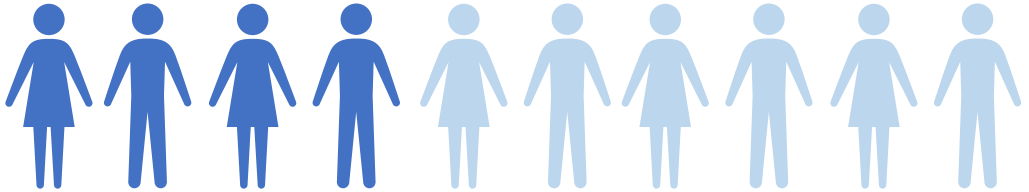
- a) Fatigue, dizziness
- b) Impaired attention, concentration or memory
- c) Negative impact on social, family, professional or academic life
- d) Mood disruption, irritability
- e) Daytime sleepiness
- f) Behavioral changes (p.ex., hyperactivity, impulsivity, agressivity)
- g) Lower motivation and energy
- h) Propensity for mistakes/accidents
- i) Lack of satisfaction about sleep quality

[†]Morin, C. M. 2020.The burden of insomnia disorders. Canadian Journal of Diagnosis (Vol 38 No.3)

[‡] DSM-IV to DSM-5 Insomnia Disorder Comparison - Impact of the DSM-IV to DSM-5 Changes on the National Survey on Drug Use and Health - https://www.ncbi.nlm.nih.gov/books/NBK519704/table/ch3.t36/

Insomnia : definition and impact

- Epidemiology
- Insomnia symptoms



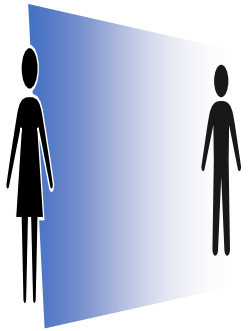
up to **40%** of the general population

Insomnia disorder

10–20%
of the general population

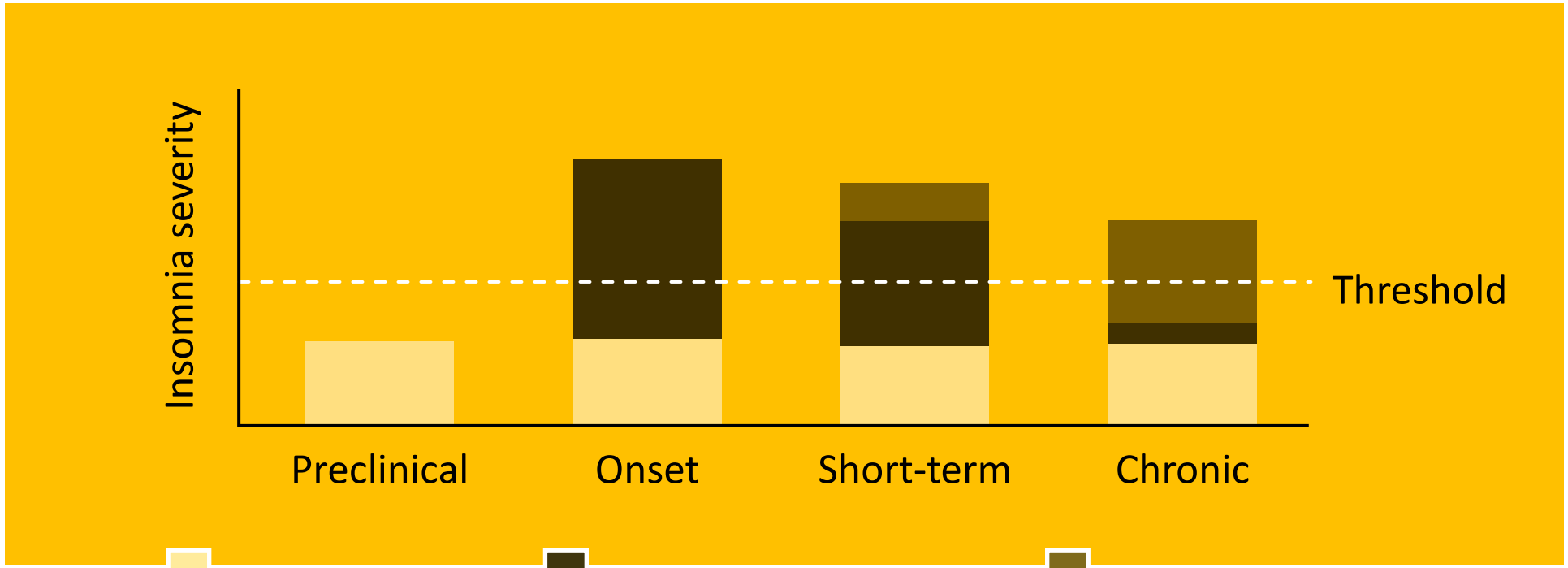
25–40%
of people > 65 yrs

Prevalence increases with age



F > M

A model for insomnia disorder



Predisposing factors

- Biological
- Psychological
- Social

Precipitating factors

- Physical illness
- Mental illness
- Stressful event

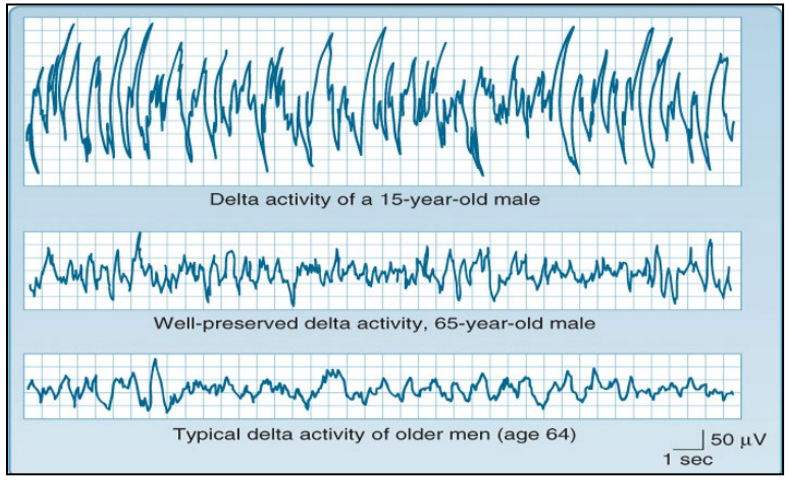
Perpetuating factors

- Excessive time in bed
- Prolonged napping
- Conditioning

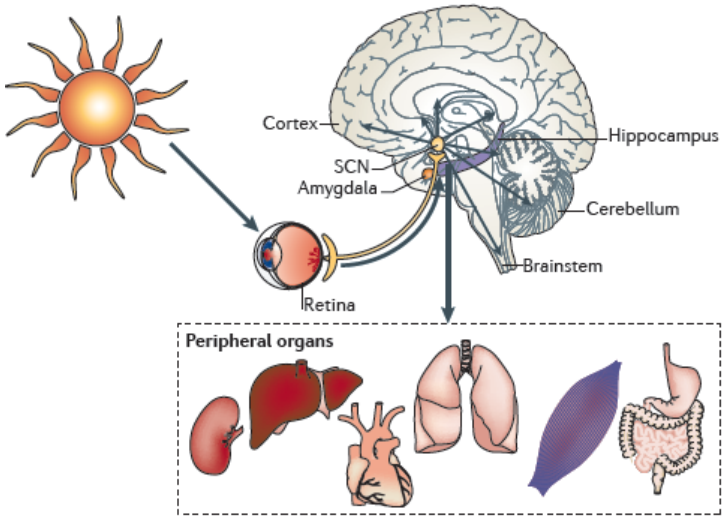
Source: Erman ML. Primary Psychiatry. Vol 14, No 7. 2007.

Insomnia disorder: Pathophysiology

- Factors related to aging
  - *Physiological factors:*
    - More prevalent comorbidities:
      - medical, neurodegenerative, other sleep disorders
    - Sleep fragmentation and reduction in deep sleep
    - Altered functioning of circadian clock



from Principles and Practice of Sleep Medicine, 2005



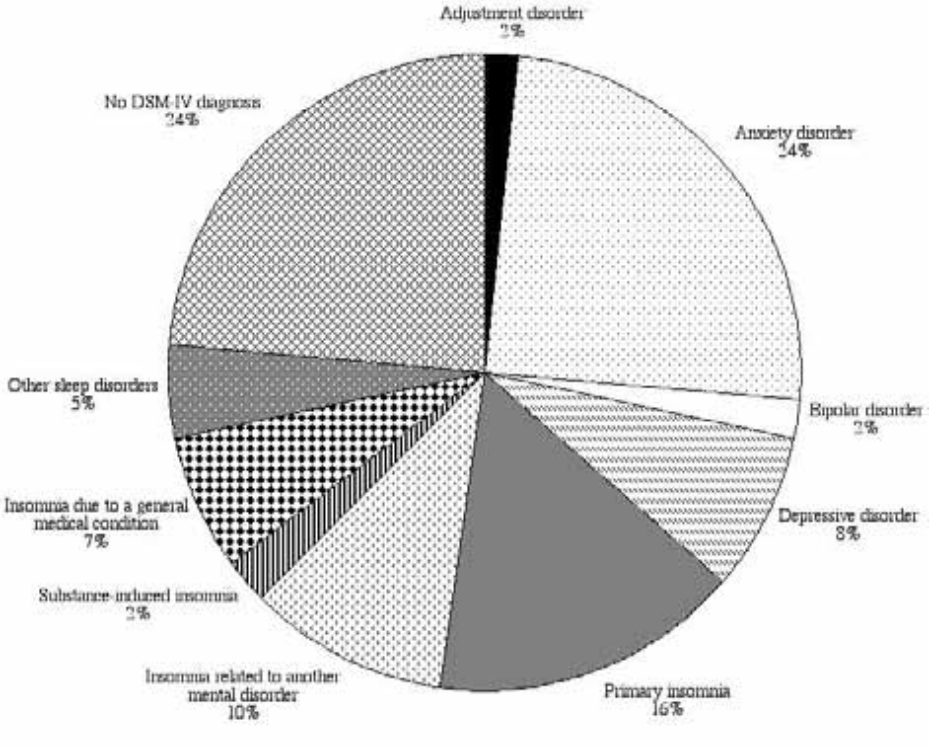
Kondratova et al, Nat Rev Neuro, 2012

Insomnia disorder: Pathophysiology

- Factors related to aging
  - *Socio-behavioral factors:*
    - Professional retirement
    - Sedentary lifestyle and prolonged naps
    - Decreased regularity in activities and sleep schedules
    - Reduced exposure to light

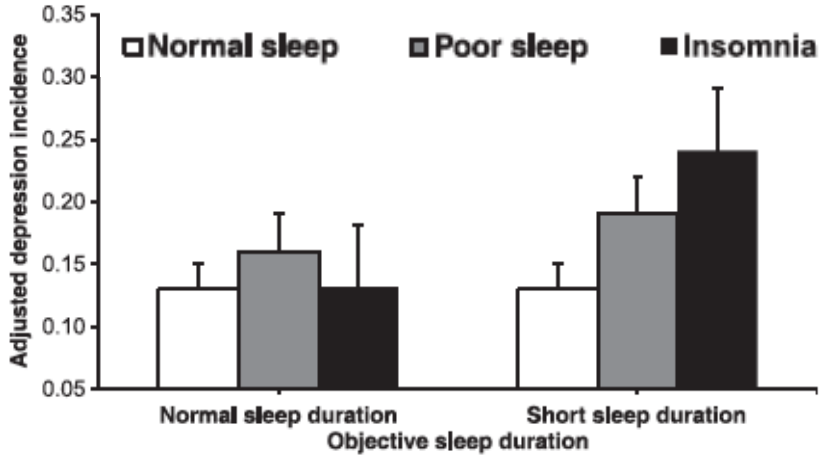
Insomnia and mental health

- ≈1/4 anxiety disorder and ≈1/10 depressive disorder
- 2-6x higher risk of developing depression (especially if sleep duration <6h) and 2-5x higher risk of developing anxiety



Depression OR (95% CI)	Anxiety OR (95% CI)
1.8 (1.6-2.0)	3.4 (3.1-3.8)

Neckelmann et al, Sleep, 2007



Fernandez-Mendoza, J Sleep Res, 2015

Insomnia and cardiovascular / metabolic health

- 2-4x higher risk of developing high blood pressure (*especially if sleep duration <6h*), 2-3x higher risk of developing diabetes and almost 2x higher of having a myocardial infarction

Table 3. Multivariable Adjusted Odds Ratio (95% CI) of Incident Hypertension Associated With Insomnia and Objective Sleep Duration

Predictors	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Normal sleep ≥6 h	1.0	1.0	1.0
Poor sleep ≥6 h	0.62 (0.33–1.18)	0.55 (0.28–1.05)	0.50 (0.26–0.98)*
Chronic insomnia ≥6 h	1.30 (0.49–3.43)	1.07 (0.40–2.88)	0.85 (0.30–2.40)
Normal sleep <6 h	0.87 (0.57–1.32)	0.88 (0.58–1.34)	0.88 (0.57–1.37)
Poor sleep <6 h	1.80 (1.04–3.12)*	1.62 (0.92–2.83)	1.34 (0.74–2.41)
Chronic insomnia <6 h	4.50 (1.96–10.3)†	3.88 (1.68–8.97)†	3.75 (1.58–8.95)*

Fernandez-Mendoza, Hypertension, 2012

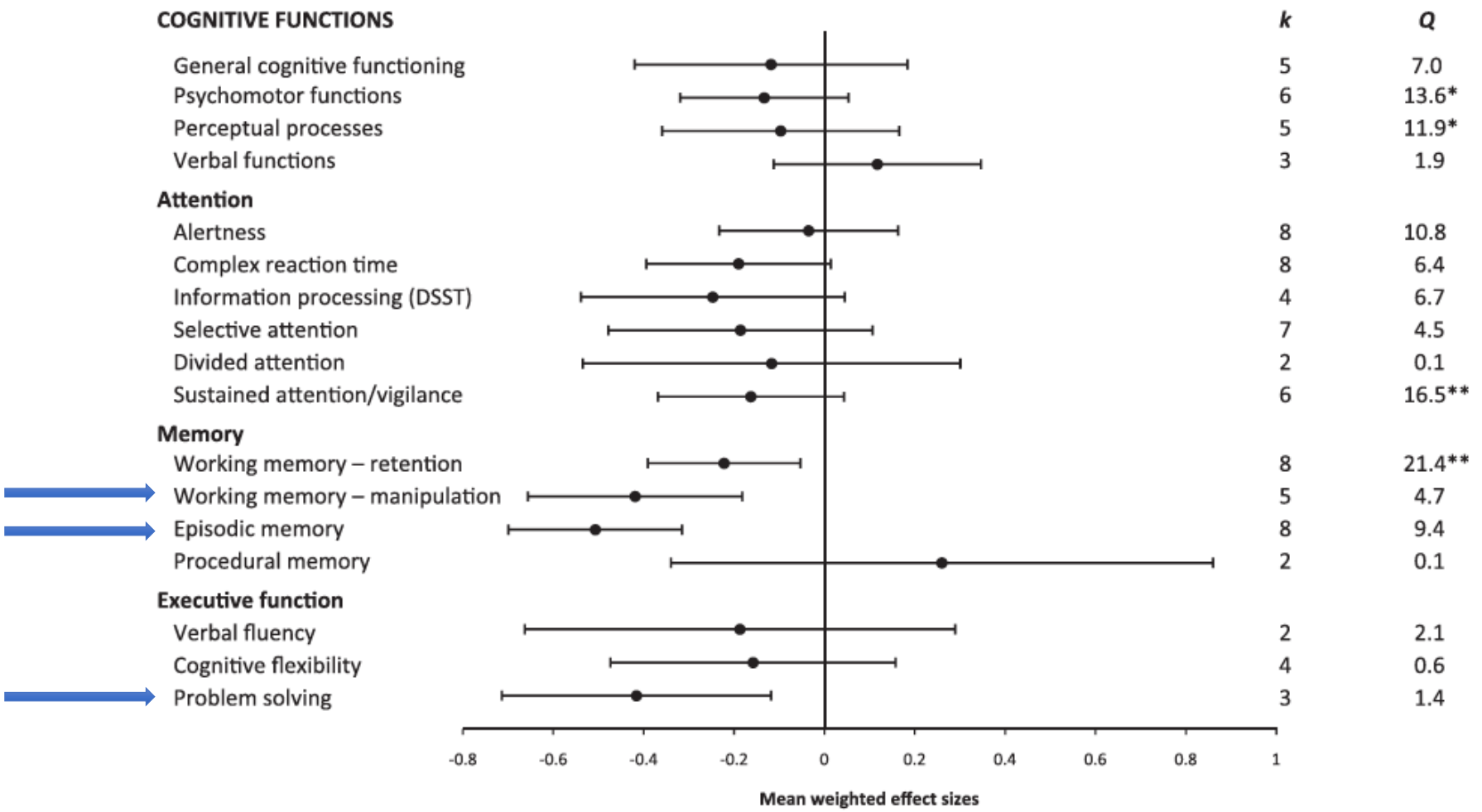
Table 3—*Multivariable adjusted ORs (95% CIs) of diabetes associated with insomnia and objective sleep duration*

Sleep difficulty and duration	Adjusted OR (95% CI)*
Normal sleeping	
>6 h	1.00
5–6 h	1.45 (0.91–2.30)
<5 h	1.10 (0.68–1.79)
Poor sleep	
>6 h	1.52 (0.87–2.65)
5–6 h	1.55 (0.80–3.01)
<5 h	1.06 (0.53–2.15)
Insomnia	
>6 h	1.10 (0.40–3.03)
5–6 h	2.07 (0.68–6.37)
<5 h	2.95 (1.24–7.03)

Vgontzas et al, Diabetes Care, 2009

Insomnia and cognitive health

Cross-sectional studies



Fortier-Brochu et al, Sleep Med Rev, 2012

Fig. 2. Average effect sizes and 95% confidence intervals by cognitive domain. Note. k = number of effect sizes available; Q = Q statistic of homogeneity. *p<.05. **p<.01. DSST; digit symbol substitution test.

Insomnia and cognitive health

Longitudinal studies

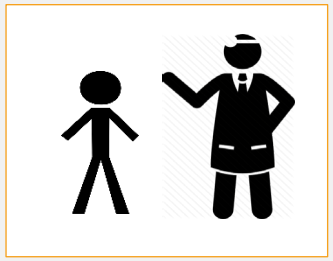
Study	N	Follow-up duration	Sleep measures	Cognitive measures	Risk
Potvin et al *(2012)*	1664	1 year	Sleep duration < 5h	MMSE	OR = 2.91 (men)
Keage et al *(2012)*	2012	10 years	Sleep duration < 6.5h	MMSE	OR = 2.02
Benedict et al *(2014)*	1029	20 years	Difficulties of falling asleep or early awakening	Alzheimer's dementia diagnosis	OR = 2.92
Sabia et al *(2021)*	7959	25 years	Sleep duration $\leq$ 6h	Dementia diagnosis	HR = 1.3

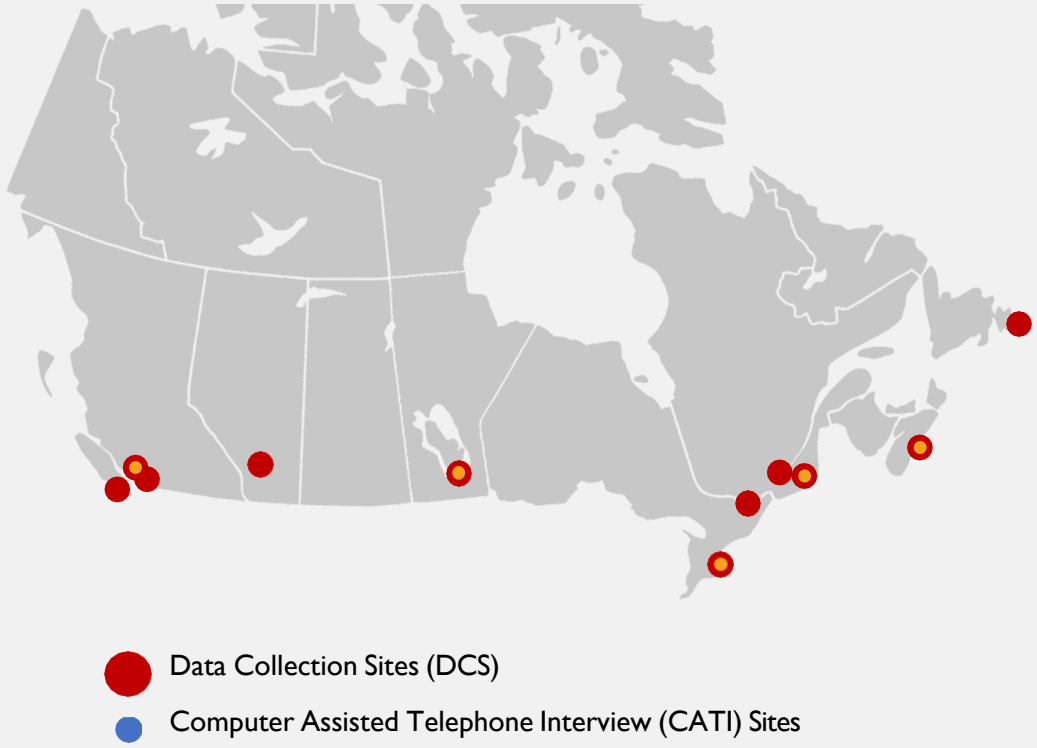
Canadian Longitudinal Study on Aging

Cross… Dang-Vu, *Sleep* , 2019

- A large national, 20-year, prospective cohort study

- **28,485 participants**
- Aim: To investigate impact of insomnia in older adults
- **Comprehensive assessments**
  - questionnaires
  - physical examinations
  - biological samples
  - neuropsychological test battery

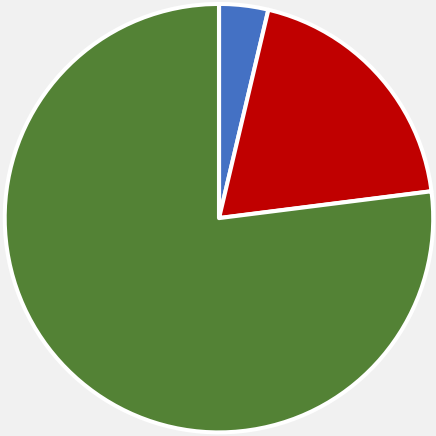




Poorer memory in older adults with insomnia disorder

Cross… Dang-Vu, *Sleep* , 2019

% of total sample



PID	ISO	NIS
1,068	5,498	21,919
3.7%	19.3%	76.9%

PID = Probable Insomnia Disorder
ISO = Insomnia Symptoms Only
NIS = No Insomnia Symptoms

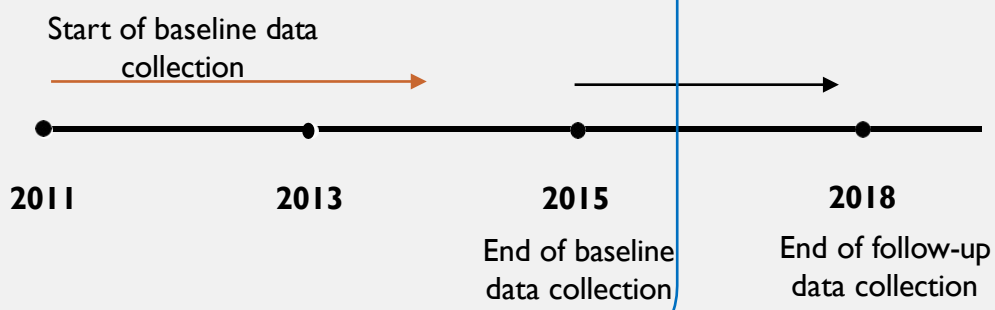
Table 1. Criteria used for categorization into PID and ISO

Criteria for PID	Criteria for ISO
Sleep onset >3× per week *OR* Sleep maintenance >3× per week *AND* Interferes with daytime function ≥ "Much" *AND* Has been present >3 months *AND* Satisfaction with sleep quality < "Neutral"	Sleep onset >3× per week *OR* Sleep maintenance >3× per week *AND* Interferes with daytime function < "Much"

Cognitive functions
Memory (RAVLT)
Executive function (MAT,STROOP,COWAT,AFT)
Psychomotor speed (CRT)
Prospective memory (TMT,PMT)

RAVLT = Rey Auditory Verbal Learning Test; MAT = Mental Alternation Test; COWAT = Controlled Oral Word Association Test; AFT = Animal Fluency Test; CRT = choice reaction time; TMT = Time-Based Prospective Memory Task; PMT = Event-Based Prospective Memory Task.

CROSS-SECTIONAL STUDY OF THE CLSA

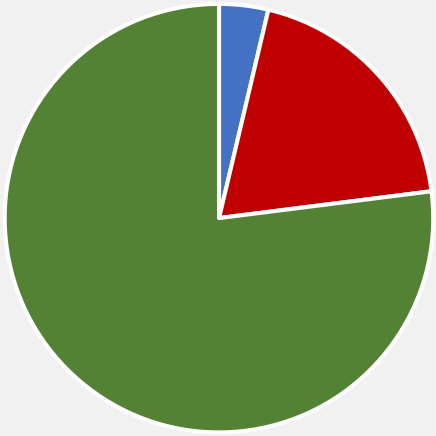


Poorer memory in older adults with insomnia disorder

SCNLab

Cross… Dang-Vu, *Sleep*, 2019

% of total sample



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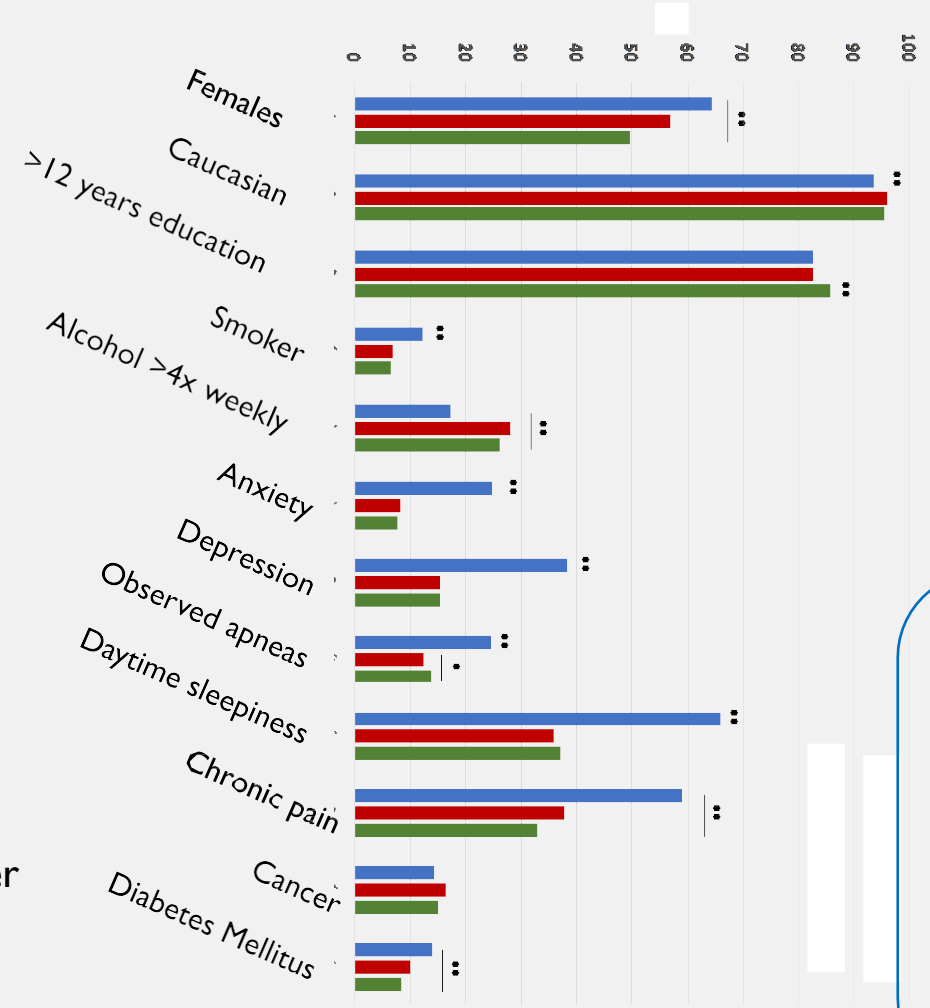
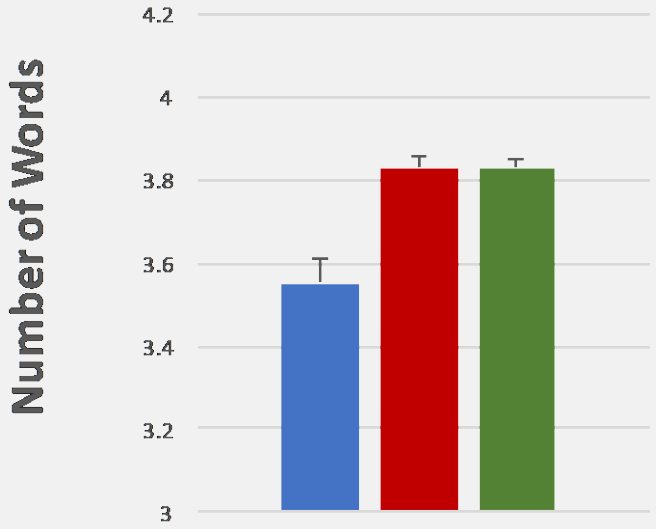
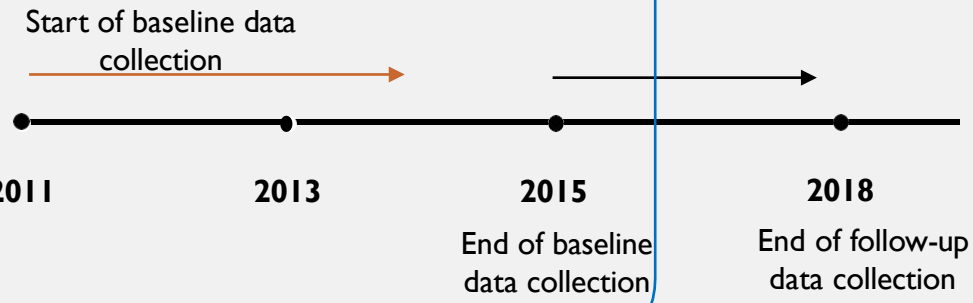


Memory test



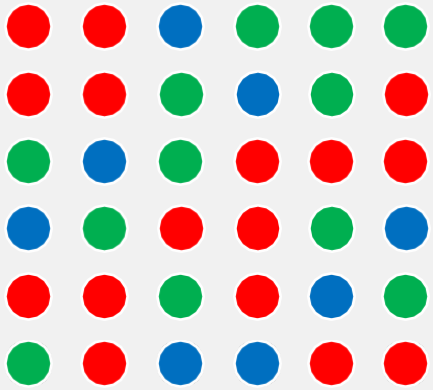
CROSS-SECTIONAL STUDY OF THE CLSA



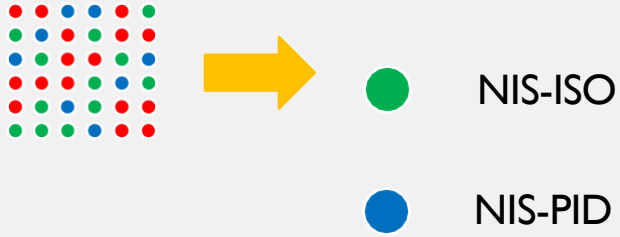
Poorer memory in older adults with insomnia disorder

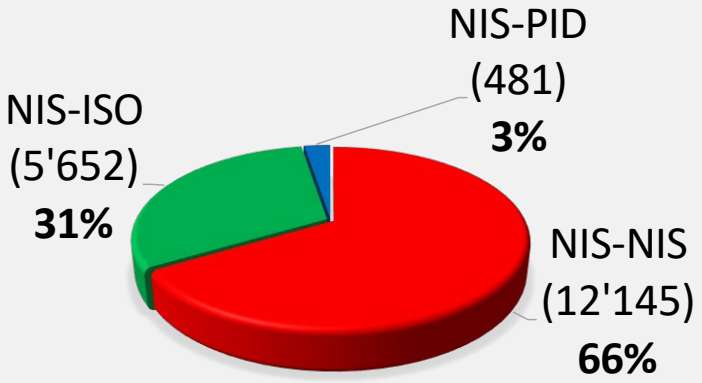
Zhao, Cross… Dang-Vu, Sleep, 2022

1. Grouping by insomnia status



2. Grouping by sleep change
(From baseline to follow-up)



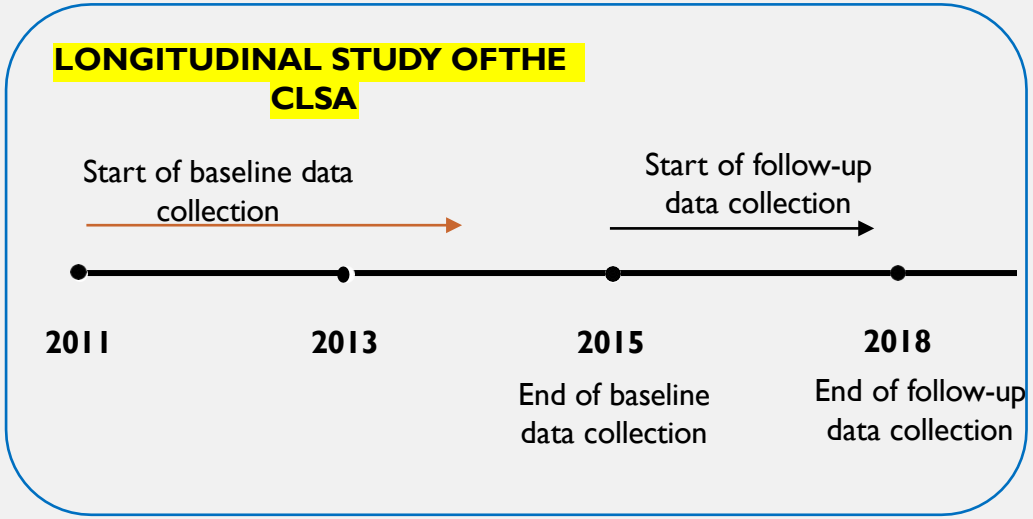


N = 18,278

PID = Probable Insomnia Disorder
ISO = Insomnia Symptoms Only
NIS = No Insomnia Symptoms

Memory assessed by:

1. Subjective memory complaint
2. Diagnosed memory problem
3. Objective memory performance
(RAVLT 1 & 2; immediate & delayed recall)



Poorer memory in older adults with insomnia disorder

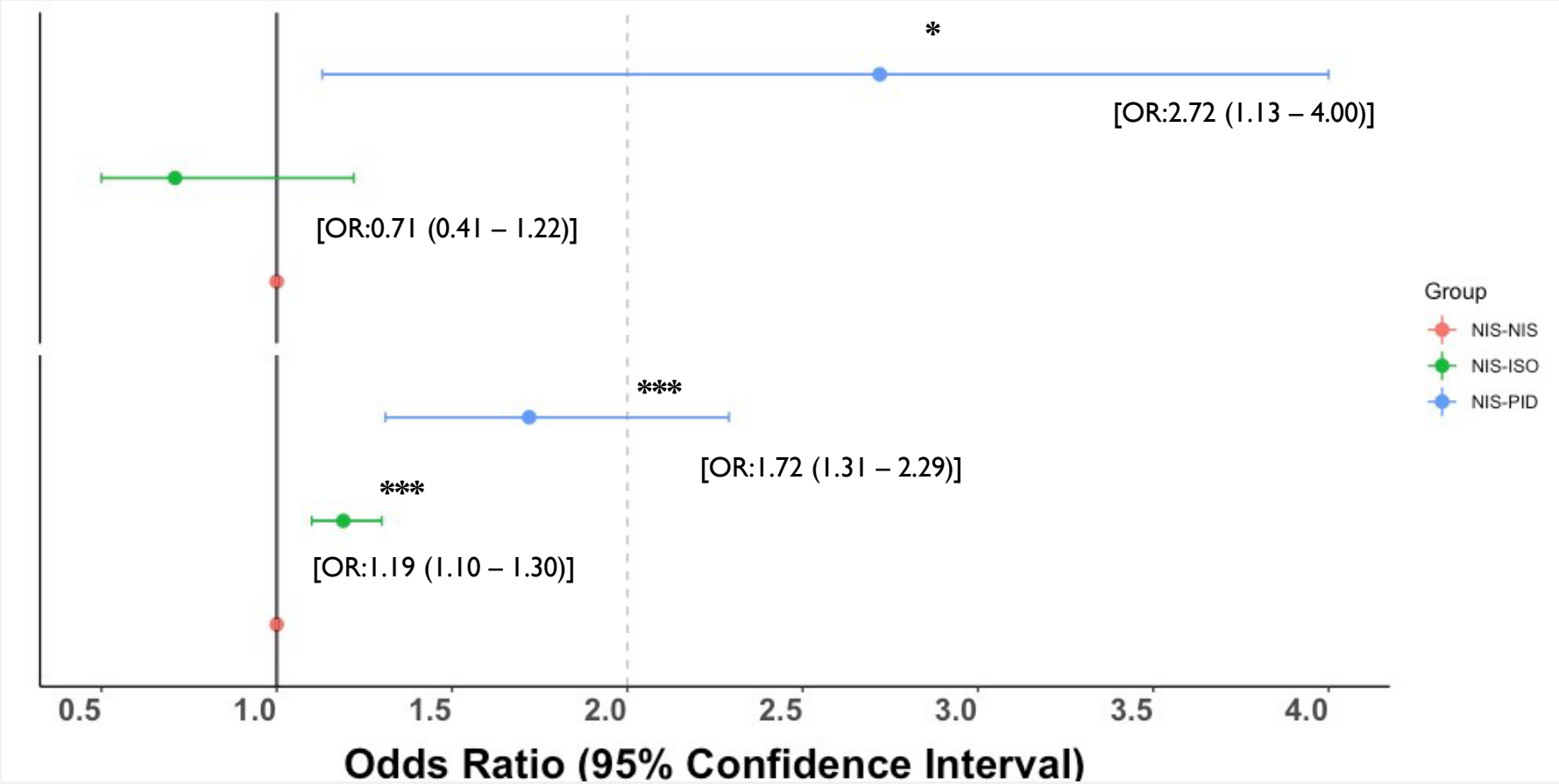
Zhao, Cross… Dang-Vu, Sleep, 2022

Reference group:
NIS to NIS

Increased odds of subjective memory decline

Diagnosed memory problem by a physician

Subjective memory worsening



Participants who developed Probable insomnia disorder (PID) showed higher odds of subjective memory decline compared to other groups, even after adjustment for comorbidities.

INSOMNIA DISORDER TREATMENT ALGORITHM

1. **Target comorbidities, drugs and consumption interfering with sleep**:
   psychiatric comorbidities (depression, anxiety), chronic pain syndrome, other associated sleep disorder (eg. sleep apnea), stimulant drugs, caffeine, alcohol

2. If #1 is insufficient, **cognitive behavioral therapy for insomnia (CBT-I)**

3. If #2 ineffective/difficult to apply: **pharmacological treatment** may be considered

Only Dual Orexin Receptor Antagonist (DORAs) are recommended for chronic use (>1 month):
Lemborexant, Daridorexant

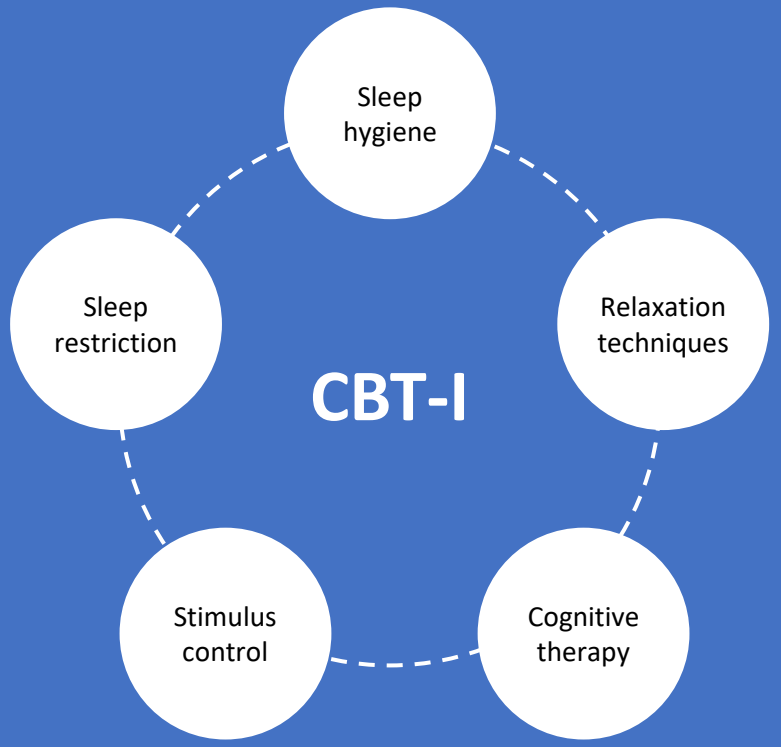
Others/acute: Benzodiazepine Receptor Agonist (Eszopiclone, Zopiclone, Zolpidem), Benzodiazepines (Temazepam), s e dative antidepressants (Doxepine)

4. **<u>Periodic reassessment</u>** and medication adjustment.

Cognitive-behavioral therapy for insomnia (CBT-I)

Objective : target factors perpetuating insomnia

- Hyperarousal
- Cognitive factors
  - *Dysfunctional beliefs*
- Behavioral factors
  - *Maladaptive behaviors*



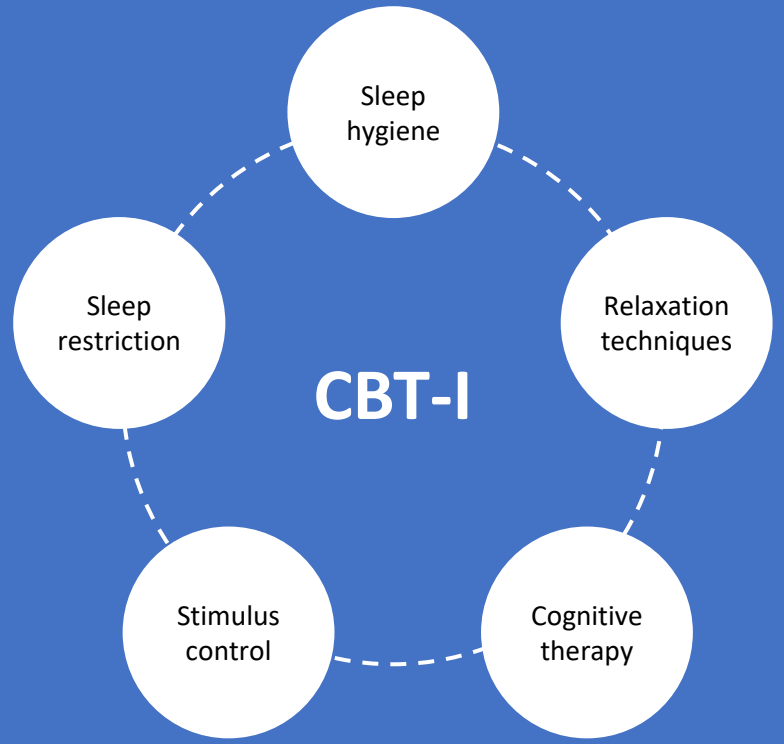
Cognitive-behavioral therapy for insomnia (CBT-I)

– Applications

Group therapy
(5–9 patients)
or individual sessions

6-8 sessions,
1 session/week
or brief therapy (1–3)

60–90 minutes/session
or customized



Cognitive-behavioral therapy for insomnia (CBT-I)

- Represents the
  first-line treatment
  for insomnia disorder:

Effective in approximately
2/3 of cases,*
including with older
patients

Long-lasting
effects

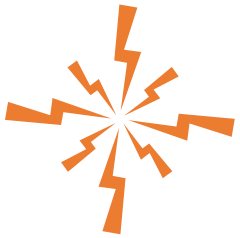
Well tolerated, no
significant adverse side
effects

** Sleep latency, duration, WASO; 40 % rémission*

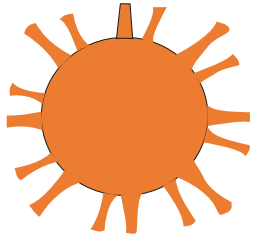
Cognitive-behavioral therapy for insomnia (CBT-I)

- Demonstrated
  efficacy
  in primary insomnia as well as comorbid insomnia such as:

Insomnia
with depression



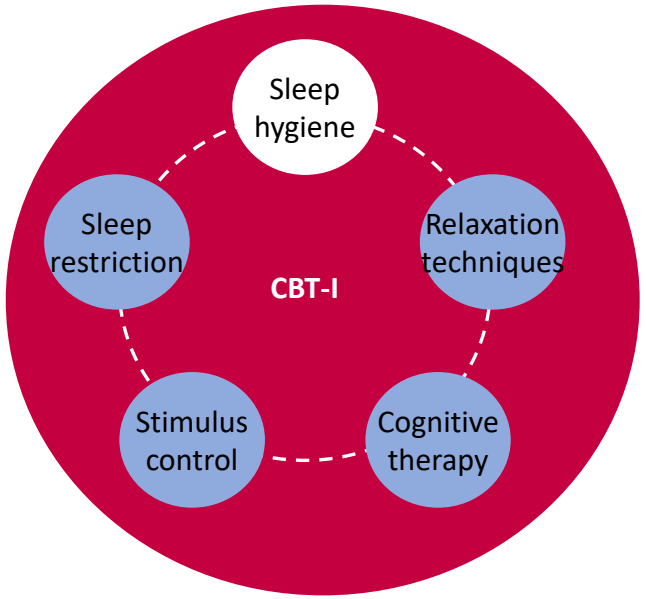
Insomnia
with chronic pain
(e.g., fibromyalgia)



Insomnia with cancer

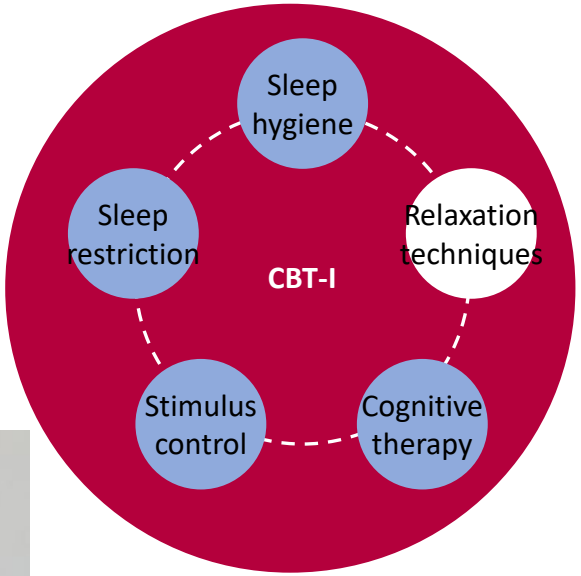
CBT-I : Sleep Hygiene

- Regular sleep schedules
- No stimulants/caffeinated beverages in the evening
- Encourage physical activity during the day:
  over 30 minutes per day (e.g., walking)
- Encourage social activities during the day
- Eat balanced meals, and avoid alcohol in the evening
- Bedroom environment
  - Quiet, dark, ventilated, not too warm (e.g. 19°C)
  - Comfortable mattress and bedding
- Avoid naps
- Maximize exposure to light during the day
  and maintain darkness at night



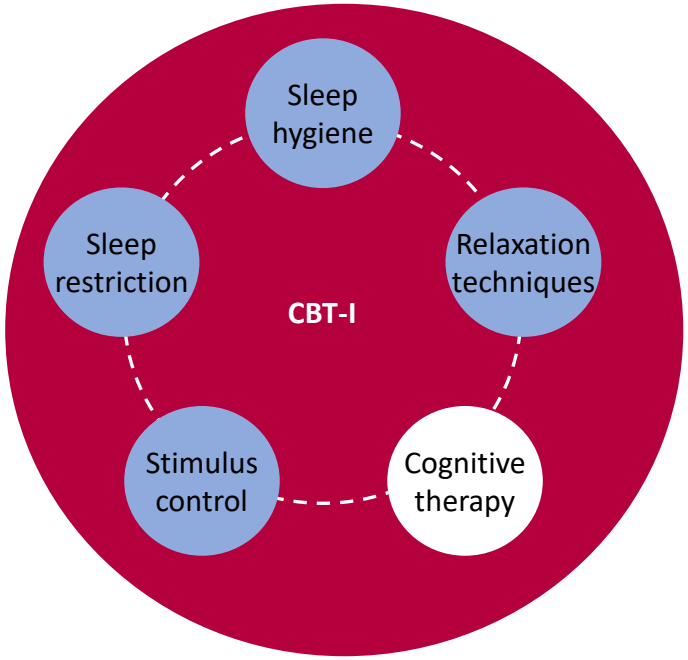
CBT-I：Relaxation

- Progressive muscle relaxation technique
- Best done near bedtime
- Customize according to patient preferences (meditation, yoga, etc.)



CBT-I: Cognitive therapy

- Targets cognitive factors that perpetuate sleep difficulties

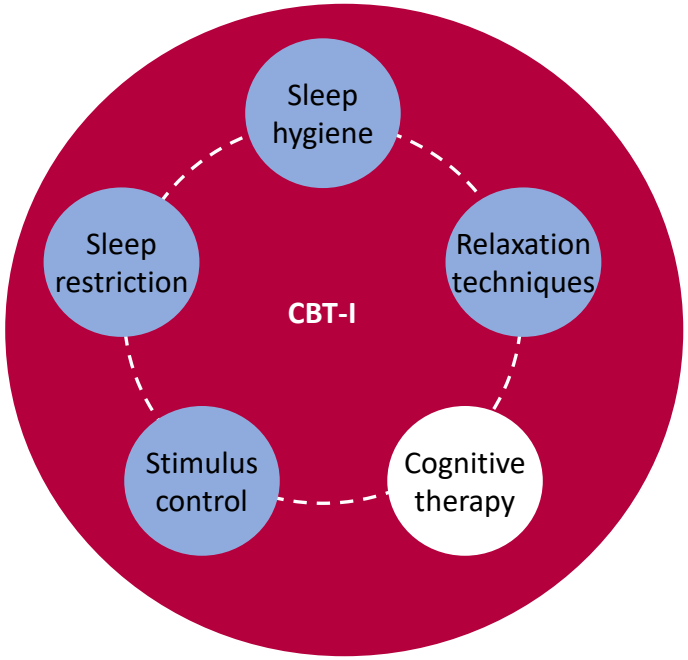


Dysfunctional beliefs about sleep

"I need to take a nap or go to bed earlier to make up for my lack of sleep"

"I absolutely need my 8 hours of sleep"

CBT-I: Cognitive therapy



- Targets cognitive factors that perpetuate sleep difficulties

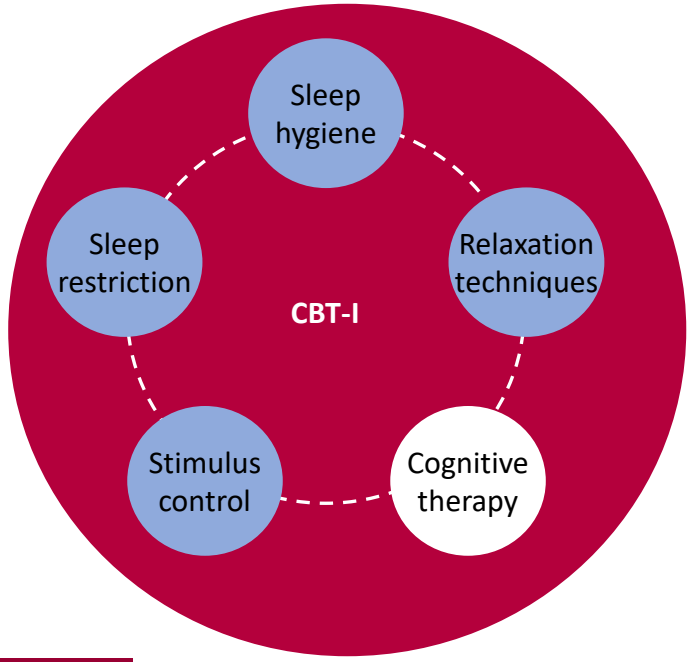
Tendency to view the consequences of insomnia as catastrophic

"One bad night could ruin my sleep schedule for the whole week"

"If I don't get a good night's sleep, I'll have to cancel my activities"

"If I don't sleep well, I won't be able to function all day"

CBT-I: Cognitive therapy



- Targets cognitive factors that perpetuate sleep difficulties

Correct dysfunctional beliefs and reappraise the impacts of insomnia

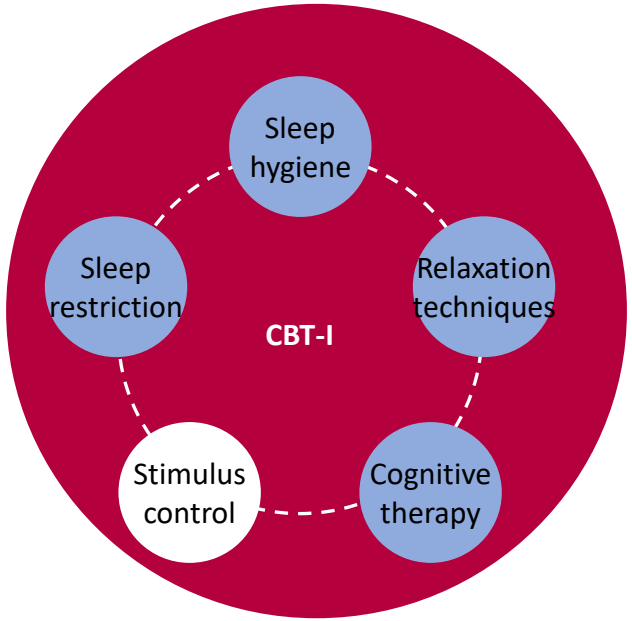
"What's the worst that could happen?"

"How have you managed it in the past?"

"How likely is that to happen?"

CBT-I: Stimulus control

- Break the association between sleep environment and hyperarousal



Only go to bed when you feel sleepy

Distinction between feeling sleepy and tired

If you're still awake after 20–30 minutes, get out of bed

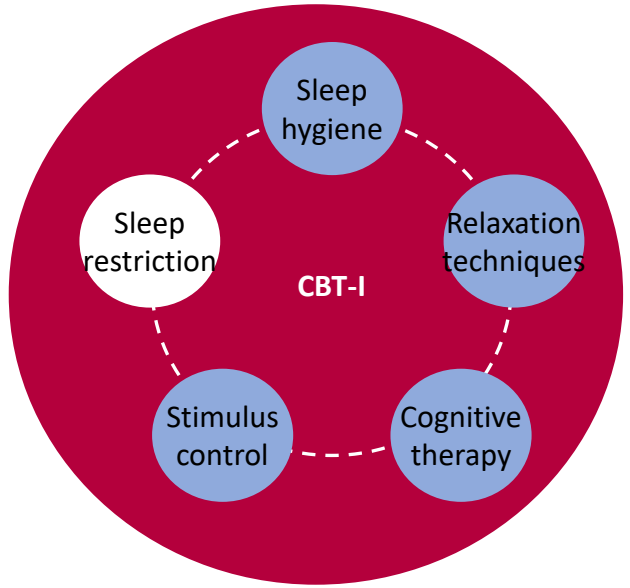
Low-stimulation activities

Go back to bed when sleepiness returns

CBT-I : Sleep restriction

- Adjust sleep schedules

- To increase sleep pressure, limit time spent in bed to average sleep time + 30 minutes



Anchor the circadian rhythm by maintaining a constant wake-up time

Once sleep is consolidated, gradually increase the amount of time spent in bed

	Mon	Tue	Wed	Thu	Fri
Time spent in bed	8:00	7:30	8:00	8:30	8:00
Sleep time	5:30	5:00	5:30	6:00	5:30

CBT-I EFFECTS ON SLEEP AND COGNITION

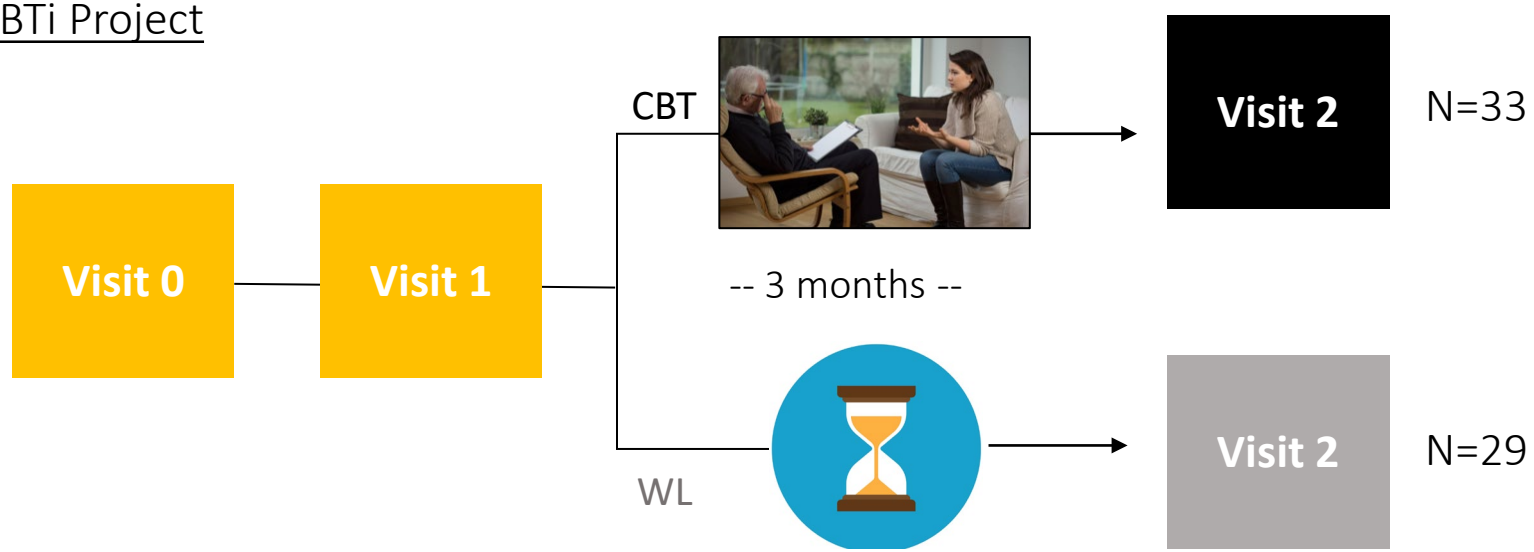
40% of the population complain of insomnia symptoms

- Difficulty to initiate and/or maintain sleep + dissatisfaction of sleep
- Daytime functioning impairment
- +10% report chronic insomnia (> 3months)

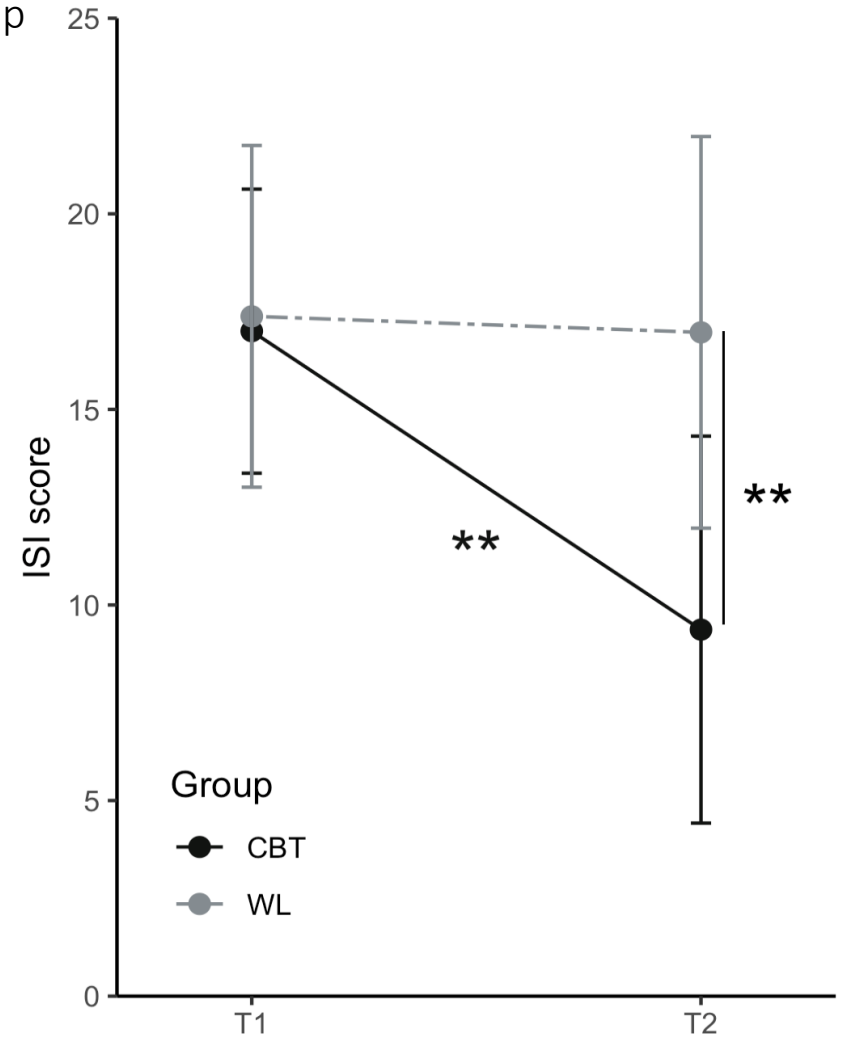
First-line treatment: cognitive behavioral treatment for insomnia (CBTi)

- Multimodal intervention focusing on maladaptive behavior and thinking patterns related to sleep
- 60% response rate (40% remission)

CBTi Project



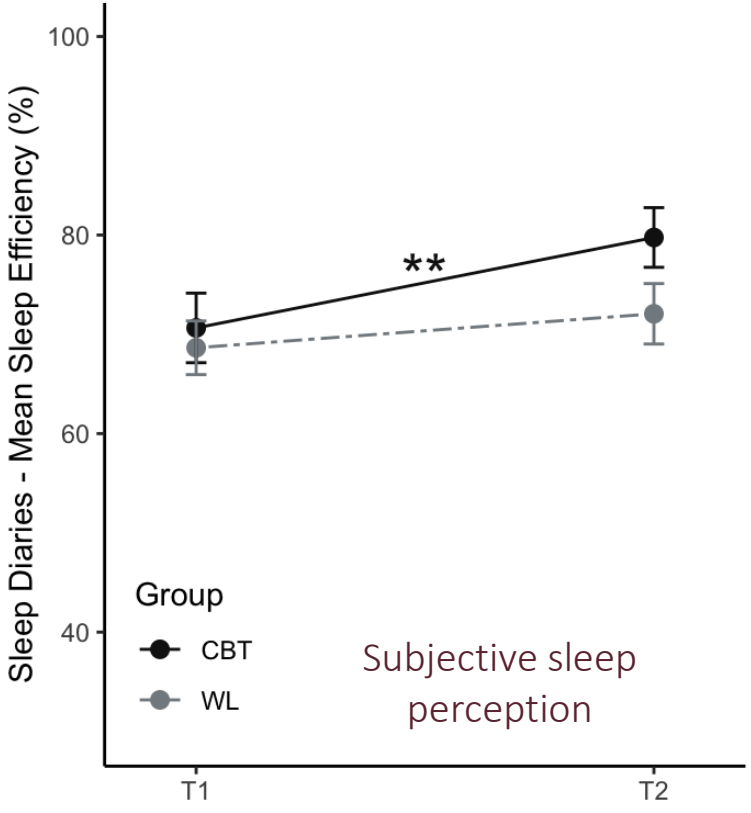
Perrault, Pomares…., Gouin, Dang-Vu, 2022, Sleep Med

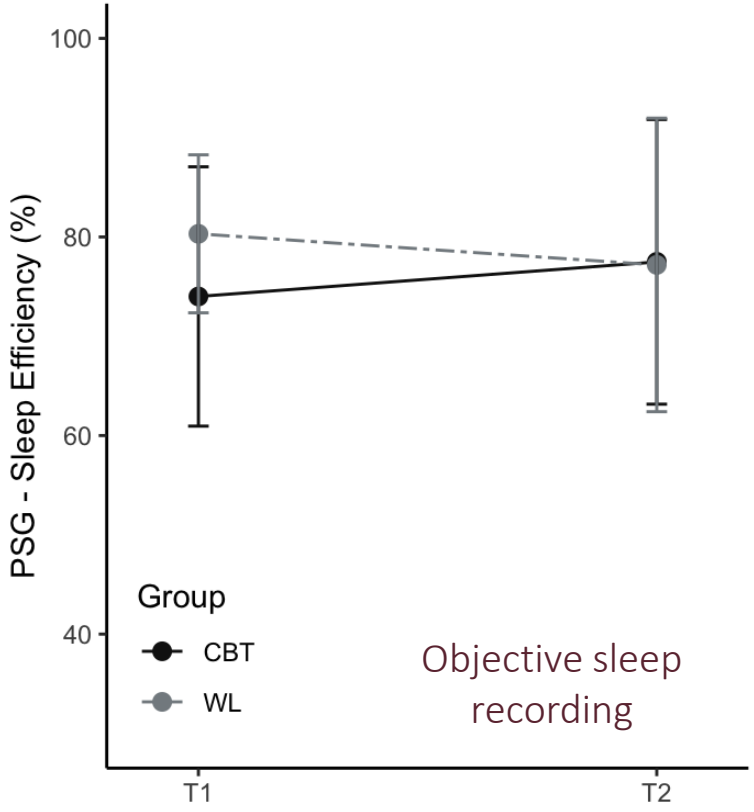


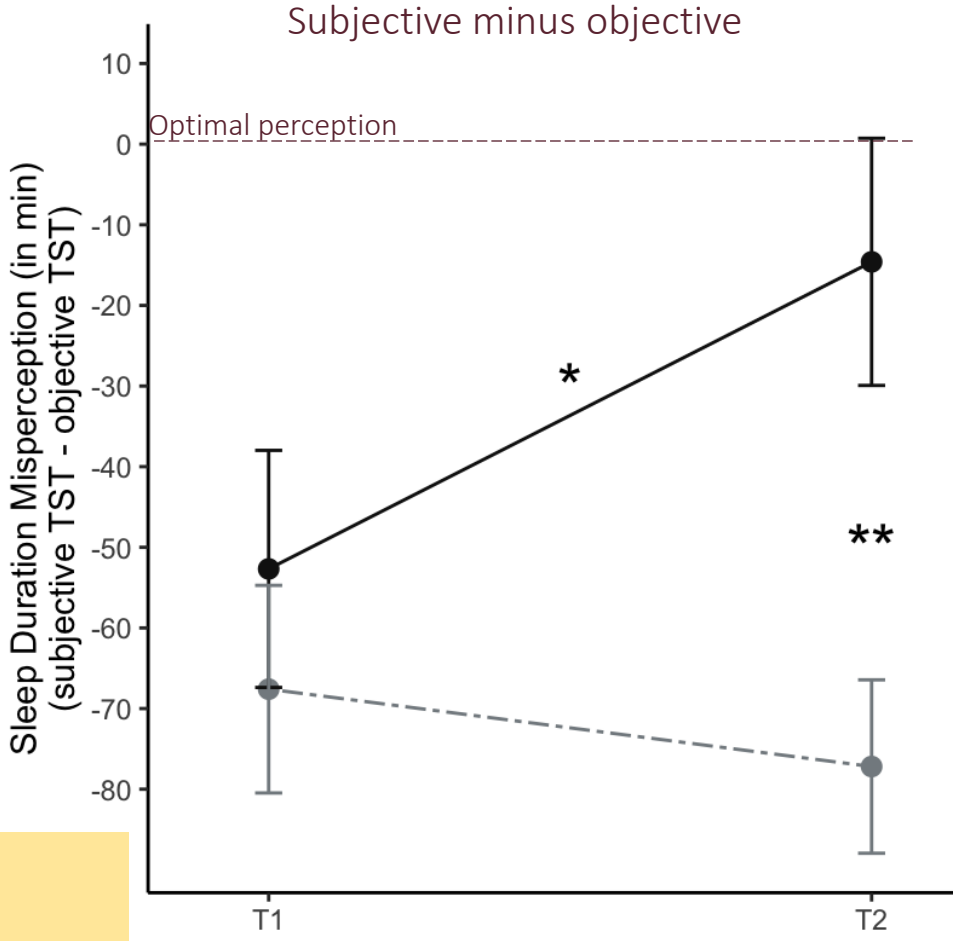
CBT-I EFFECTS ON SLEEP AND COGNITION

Multimodal assessment of CBTi efficacy on sleep using subjective and objective methods

Perrault, Pomares…., Gouin, Dang-Vu, 2022, Sleep Med







Compared to a wait-period, CBTi:

- Improve subjective perception of sleep (sleep latency, time spent awake, sleep quality)
- But no objective change
- Thus reduce discrepancy between subjective and objective measures (sleep misperception)

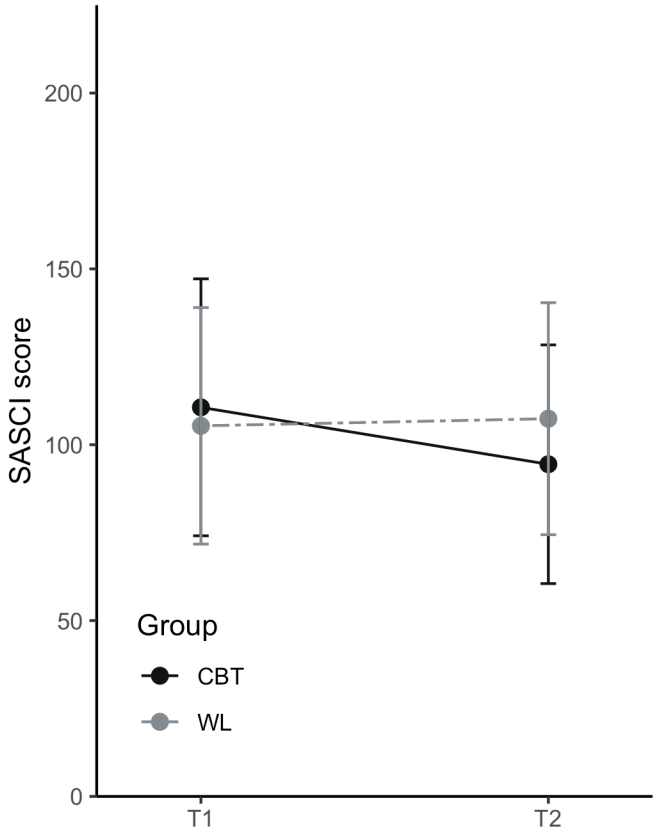
CBT-I EFFECTS ON SLEEP AND COGNITION

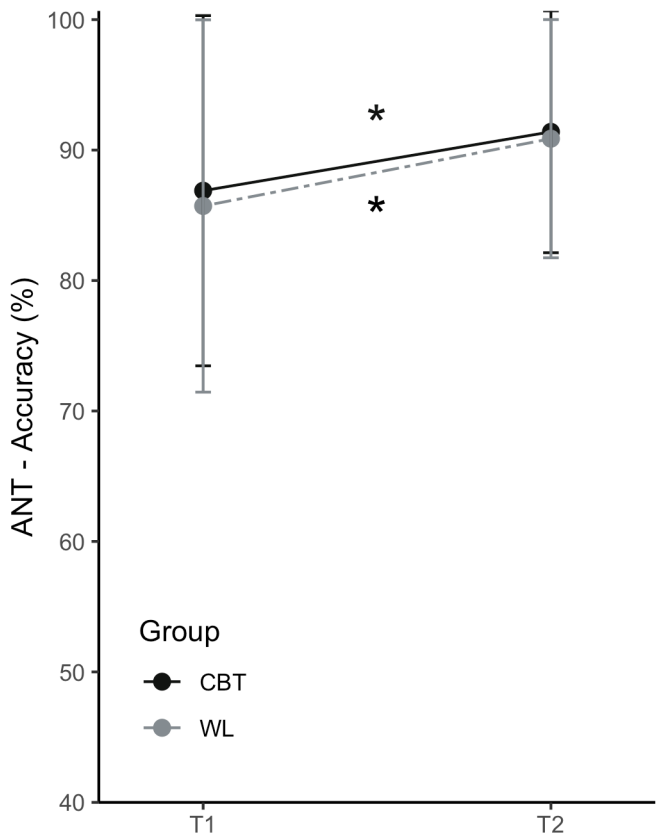
Multimodal assessment of CBTi efficacy on cognition using subjective and objective methods

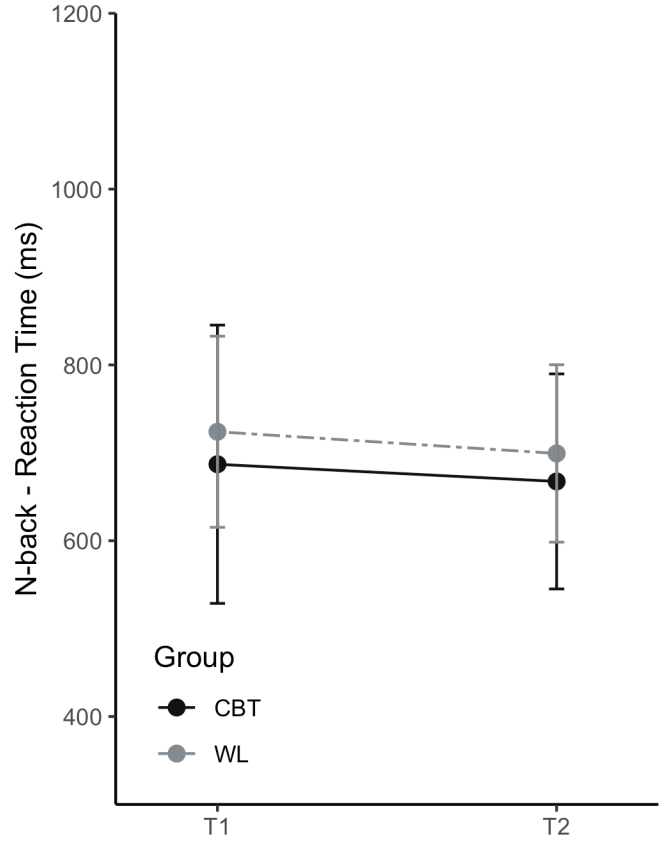
Perrault, Pomares…., Gouin, Dang-Vu, 2022, Sleep Med

Subjective cognitive abilities

-------- Objective cognitive performance --------







Compared to a wait-period, CBTi:

- Trend to improve subjective perception of cognitive abilities (p=0.07)
- But no objective change

e-COSMOS study

Centre de recherche iugm
Institut universitaire de gériatrie de Montréal

Improving sleep to protect brain health in older adults:

Assessing a novel cognitive-behavioral program for insomnia using a multidomain web platform

OBJECTIVE

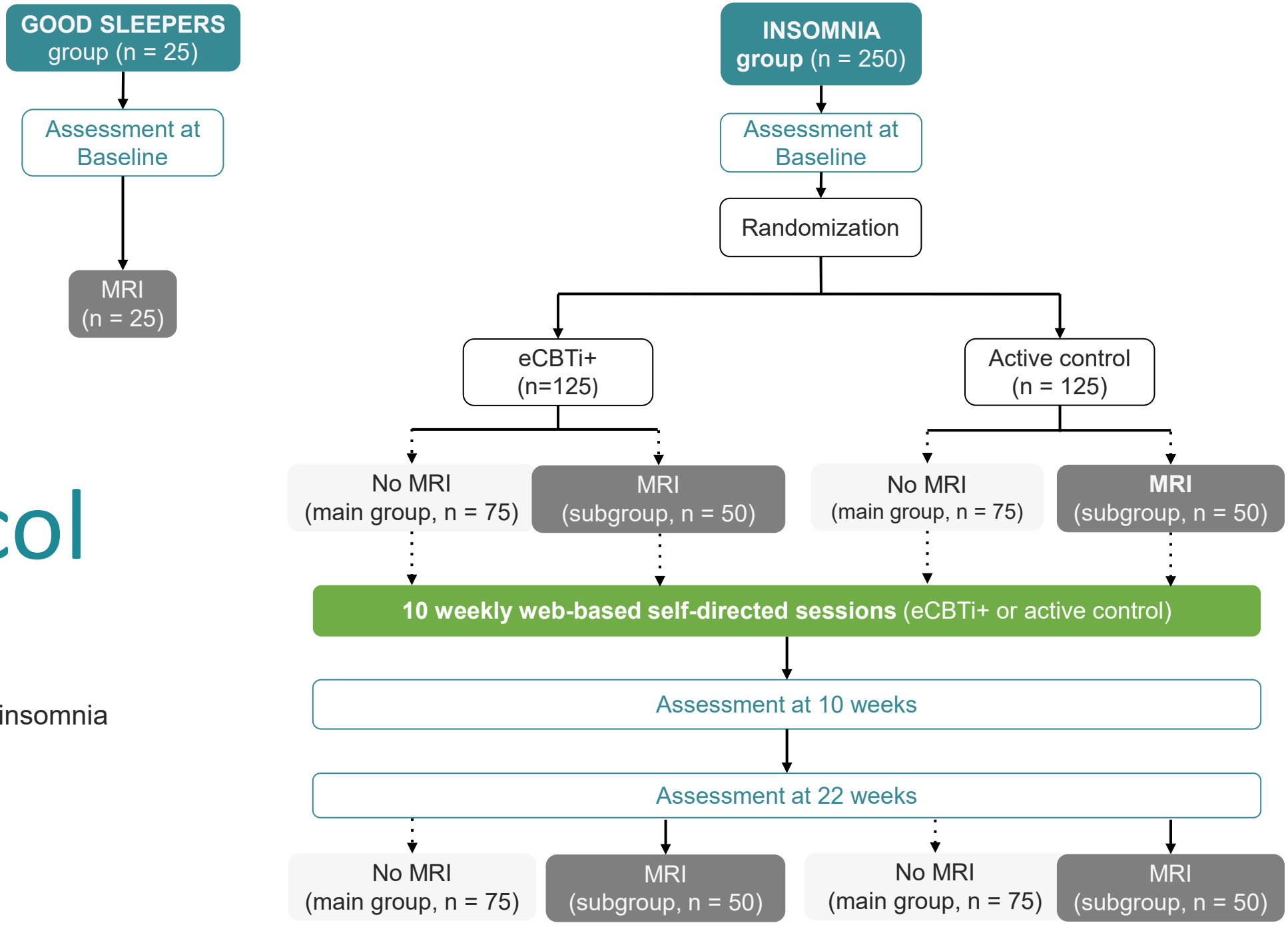
Assess the effectiveness of eCBTi+ on sleep, mental health, and brain health in older adults with insomnia disorder and subjective cognitive complaints

Protocol

2 groups

250 participants with insomnia

25 good sleepers



Inclusion criteria

Inclusion criteria

- Age 60 years or older
- With insomnia disorder
- With subjective cognitive decline
- Living in Quebec or Ontario
- Able to use a smartphone, tablet or computer
- Having access to home internet connection

Contact us
(514) 340-3540, ext. 4790
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Medications Indicated/Approved for the Treatment of Insomnia in Canada

GABAergic Sedatives

Class	Drugs	Indication(s)	
		Sleep onset	Sleep maintenance
Benzodiazepines (BZD) $GABA_A$ receptor agonists	**Temazepam**	✓	✓
Non-BZD Receptor Agonists (Z-Drugs) $GABA_A$ receptor agonists	**Zopiclone** (e.g., Imovane) **Zolpidem** (e.g., Sublinox) **Eszopiclone** (Lunesta)	✓ ✓ ✓	✓ ✓
Tricyclic Antidepressant H_1 antagonist	**Doxepin** (Silenor)		✓
Orexin receptor antagonists	**Lemborexant** (Dayvigo) **Daridorexant** (Quviviq)	✓ ✓	✓ ✓

Conclusion

Insomnia disorder

- is very common, with a major impact on physical, mental and cognitive health

Cognitive behavioral therapy for insomnia (CBT-I)

- is the first-line treatment for chronic, primary or comorbid insomnia in older adults
- is effective in both short- and long- terms
- targets inappropriate beliefs and behaviors perpetuating insomnia
- can be customized and administered at different levels of intervention (accessibility)

Pharmacotherapy

- first line : Lemborexant, Daridorexant, Eszopiclone, Zopiclone, Zolpidem, Temazepam, Doxepin
- chronic use: only Lemborexant and Daridorexant recommended
- especially when CBT-I is ineffective, not accessible or not applicable

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Research Laboratory **https://scnlab.com/**

SCNLab
SLEEP, COGNITION AND NEUROIMAGING LABORATORY

cshn

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- **Useful resources**
(information for patients and professionals)

- Canadian Sleep Society

https://scs-css.ca

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Fonds de recherche Santé Québec

CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

NSERC CRSNG

Weston Family Foundation

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