



UCSF Weill Institute for Neurosciences

Memory and Aging Center

UNRAVELING SLEEP IN AGING

San Francisco Towers

Christine M Walsh, PhD

Associate Professor

Sleep in Aging & Neurodegenerative Disease Program

Memory & Aging Center, Department of Neurology, Weill Institute for Neurosciences

University of California, San Francisco

COLLABORATORS & FUNDING

UCSF SAND lab

Thomas Neylan
Lea Grinberg
Joseph Oh
Quentin Coppola
Michael Le
Natalie Pandher
Leslie Yack
AJ Simon
Grinberg Lab

MAC UCSF teams

4RTNI, ADRC, Aging, ALLFTD,
RabLab, Grinberg Lab, PPG,
PSDC, RPD, Trials

UCSF

Adam Boxer
Kaitlin Casaletto
Doris Chen
Michael Geschwind
Hilary Heuer
Mary Koestler
Joel Kramer
Andrew Krystal
Bruce Miller
Gil Rabinovici
Kamalini Ranasinghe
Julio Rojas
Niyatee Samudra
Wade Smith
Adam Staffaroni
Sara Timtim
Lawren VandeVerde

Mayo Clinic- Rochester

Erik St Louis
Bradley Boeve

UCLA

Keith Vossel

Hospital Clinic, Barcelona

Neus Falgàs

Stanford University

Emanuel Mignot
Jenny Zitser

Advanced Brain Monitoring, Inc

Funding:

Rainwater Charitable Foundation
Hillblom Foundation Network Grant
NIA R01 AG032289 (Kramer)
NIA RO1 AG038791 (Boxer)
NIA U54NS092089 (Boxer)
NIA R01AG060477 (Neylan, Grinberg)
NIA R01 AG064314 (Grinberg, Neylan)

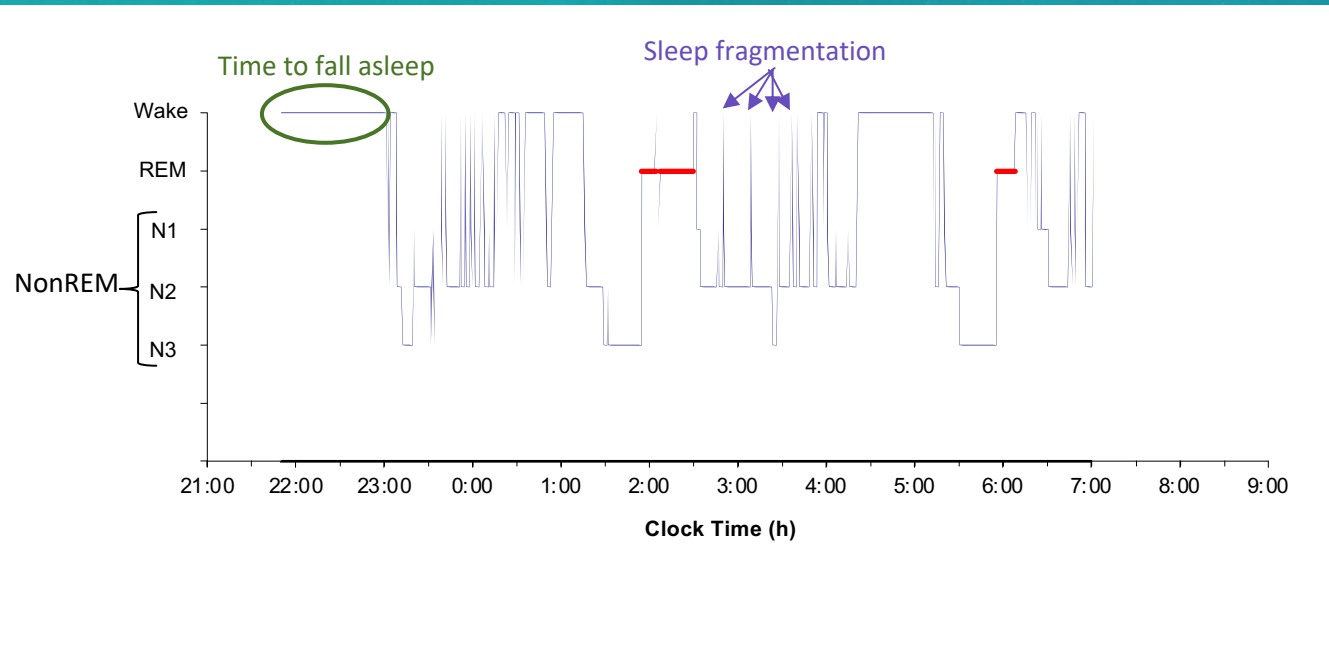
Participants, Families & Careteams

Contact: Christine.walsh@ucsf.edu
No conflicts of interest

SEMINAR'S FOCUS

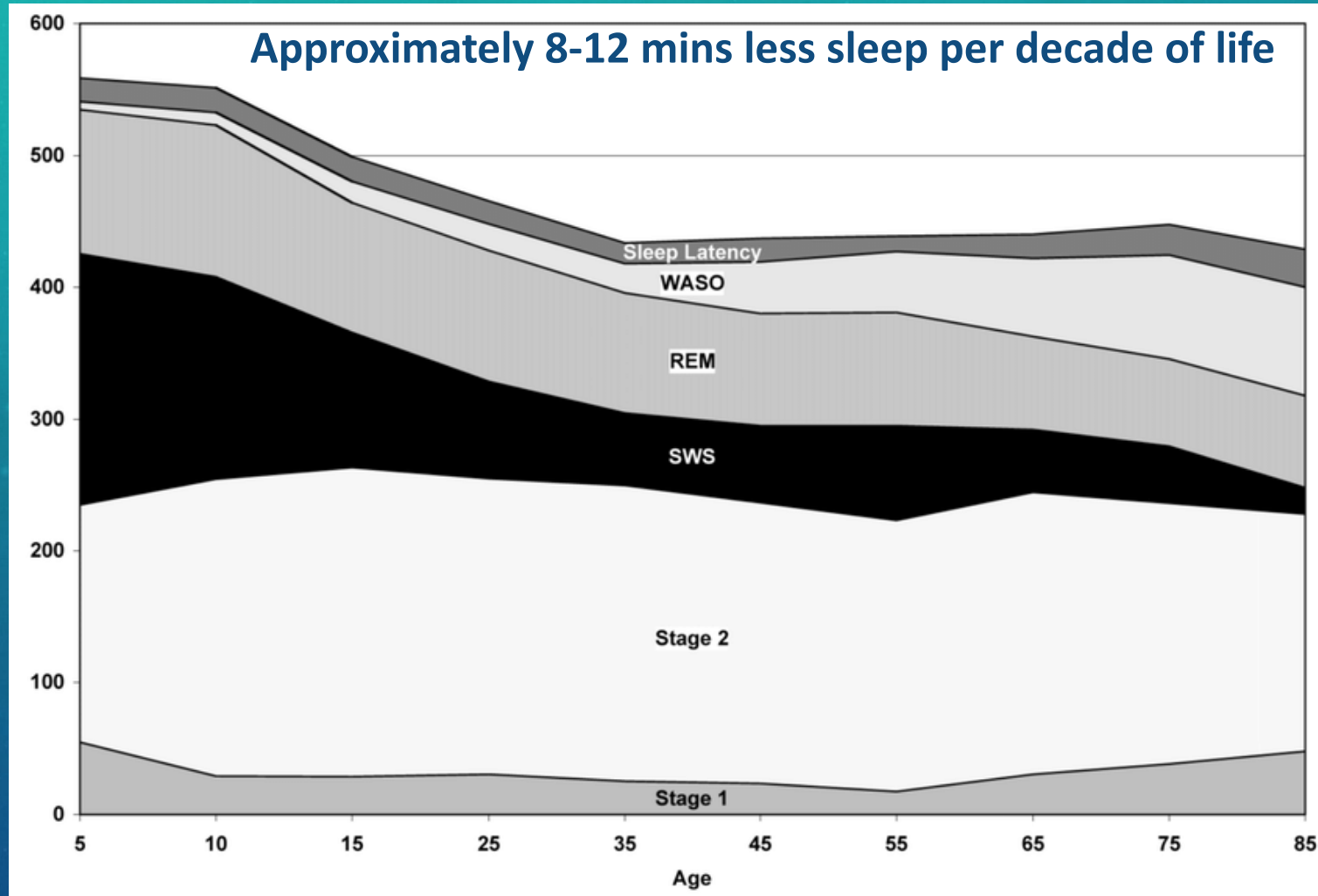
- General benefits of sleep/ general health associations
- How is sleep loss associated with the brain
- Can sleep be a contributor to neurodegenerative disease?
- Sleep hygiene and tips

FUNCTION OF SLEEP



- As protection
- To thermoregulate
 - Internal temperature decreases during sleep
 - Possible role in heat retention
- To conserve metabolic energy
 - 15% less energy than quiet waking
 - Restorative
- To regulate hormones
 - E.g. ghrelin and insulin
- To regulate the immune system
- To support cognition & mental health

WHAT IS THE IDEAL DURATION OF SLEEP?



- Guideline: 7.5 hrs of sleep

Ohayon et al., 2004; Dorffner et al., 2015; Floyd et al., 2000; Floyd et al., 2000

SUBJECTIVE SLEEP QUALITY AND OLDER ADULTS

- Up to 50% of older adults may have poor sleep (Vitiello et al., 2004; Luo et al., 2013)
 - Typically associated with comorbidities (Vitiello et al., 2004; Foley et al., 1999)
- 34% older adults are poor estimators of their sleep duration (Raikes et al., 2018)
- Among non-complainers, 33% women and 16% men had disrupted sleep (Vitiello et al., 2004)
- Poor subjective sleep quality associated with middle of the night awakenings more so than time to fall asleep (Zitser et al., 2022)
- Healthy older adults are less likely to report poor sleep than young adults (Gooneratne et al., 2011)

In young adults
reaction times after
24 hrs awake

=

0.085 % blood alcohol concentration
(Dawson & Reid, 2007)

14 days of 6hrs sleep/night

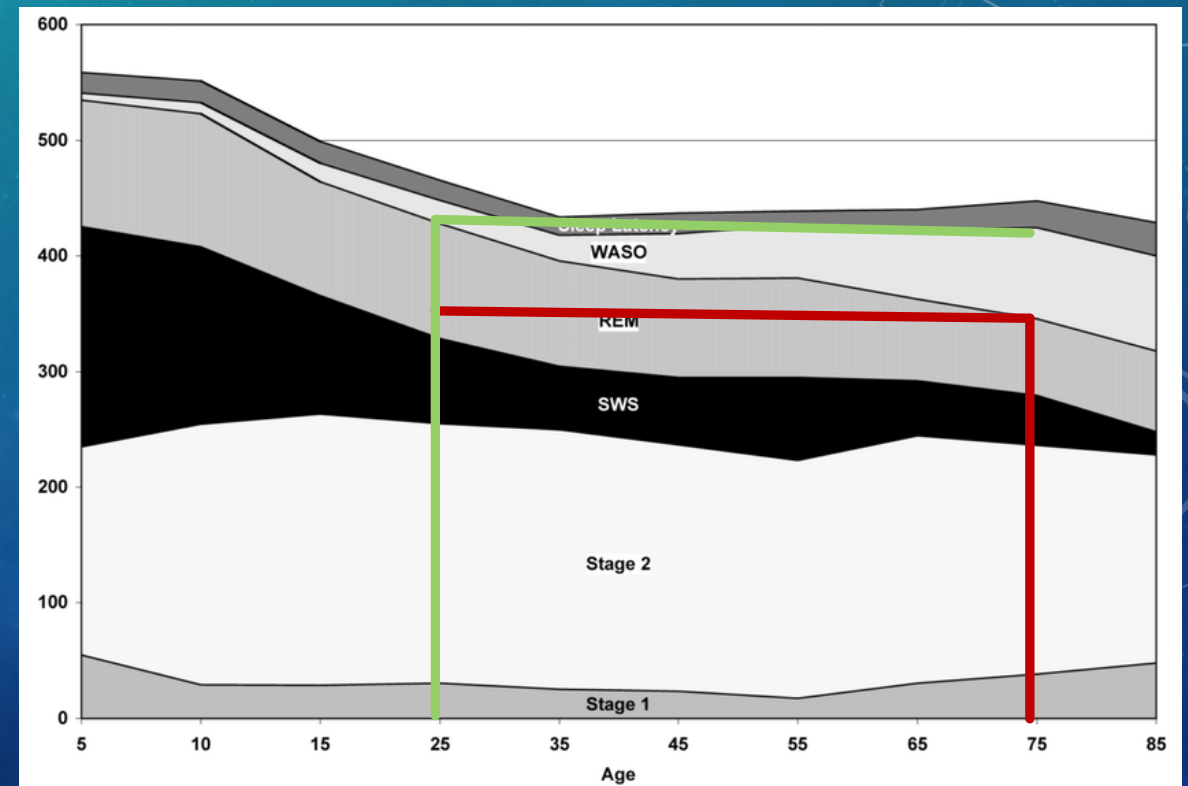
=

2 days of complete sleep deprivation
(van Dongen et al., 2003)

Older adults are less affected by sleep
deprivation than young adults

(Duffy et al., 2007)

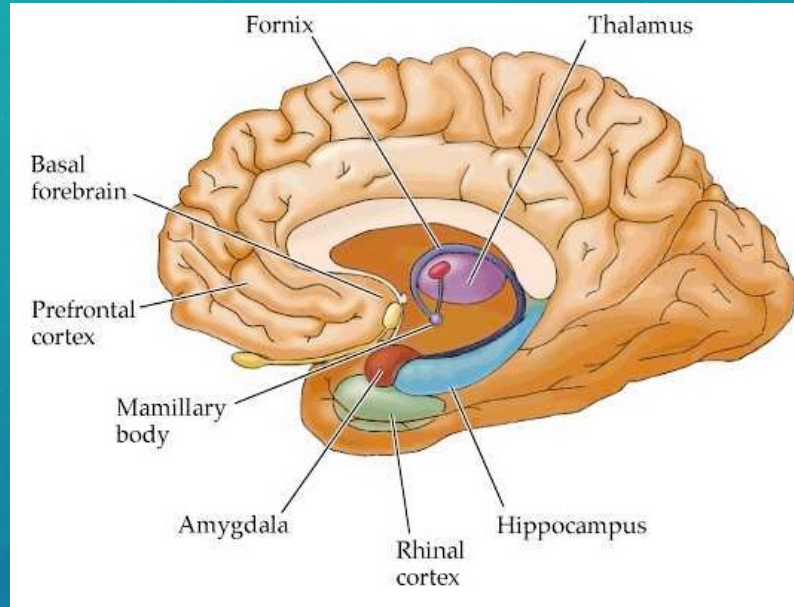
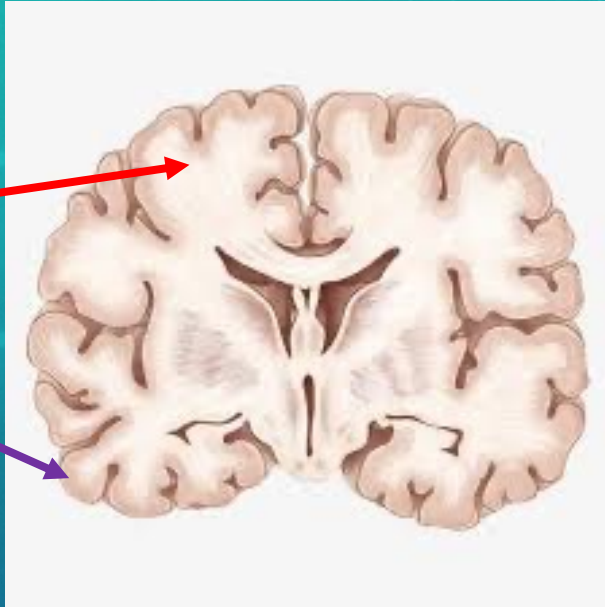
~~“Older adults need less sleep”~~



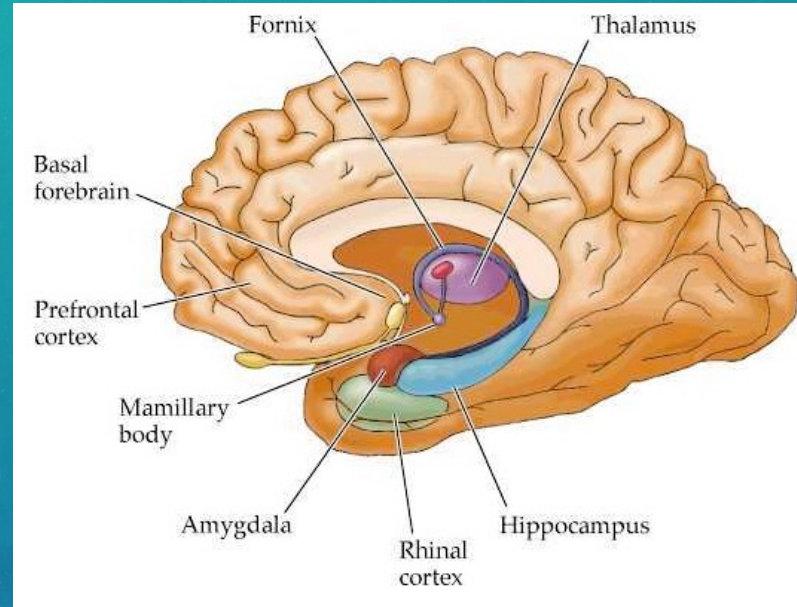
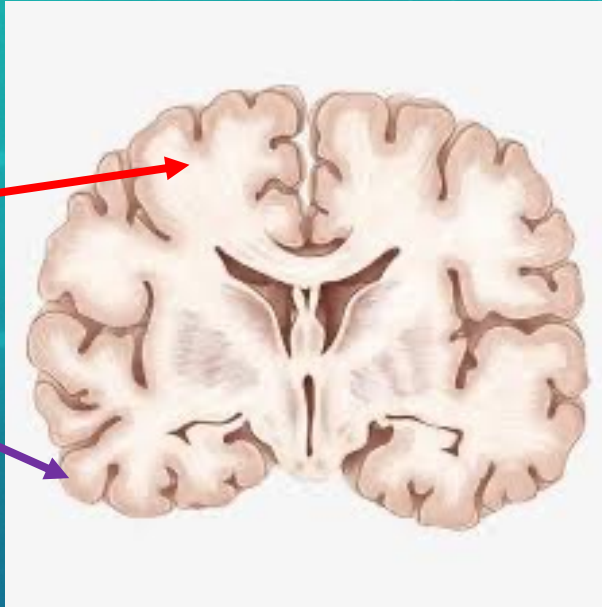
TOO MUCH SLEEP CAN BE A BAD THING

- Can be an indicator for
 - Cardiometabolic disease
 - Depression
 - Cognitive impairment
- Individuals carrying the APOe4 gene who napped more than 60 mins a day were more likely to later receive a diagnosis of Alzheimer's disease (Asada et al., 2000)

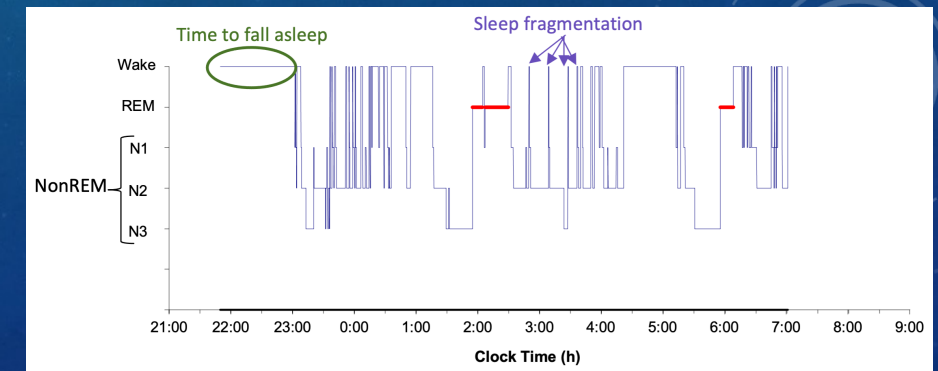
WHITE MATTER VS GRAY MATTER IN THE BRAIN



DOES IT MATTER HOW WE THINK WE SLEEP?

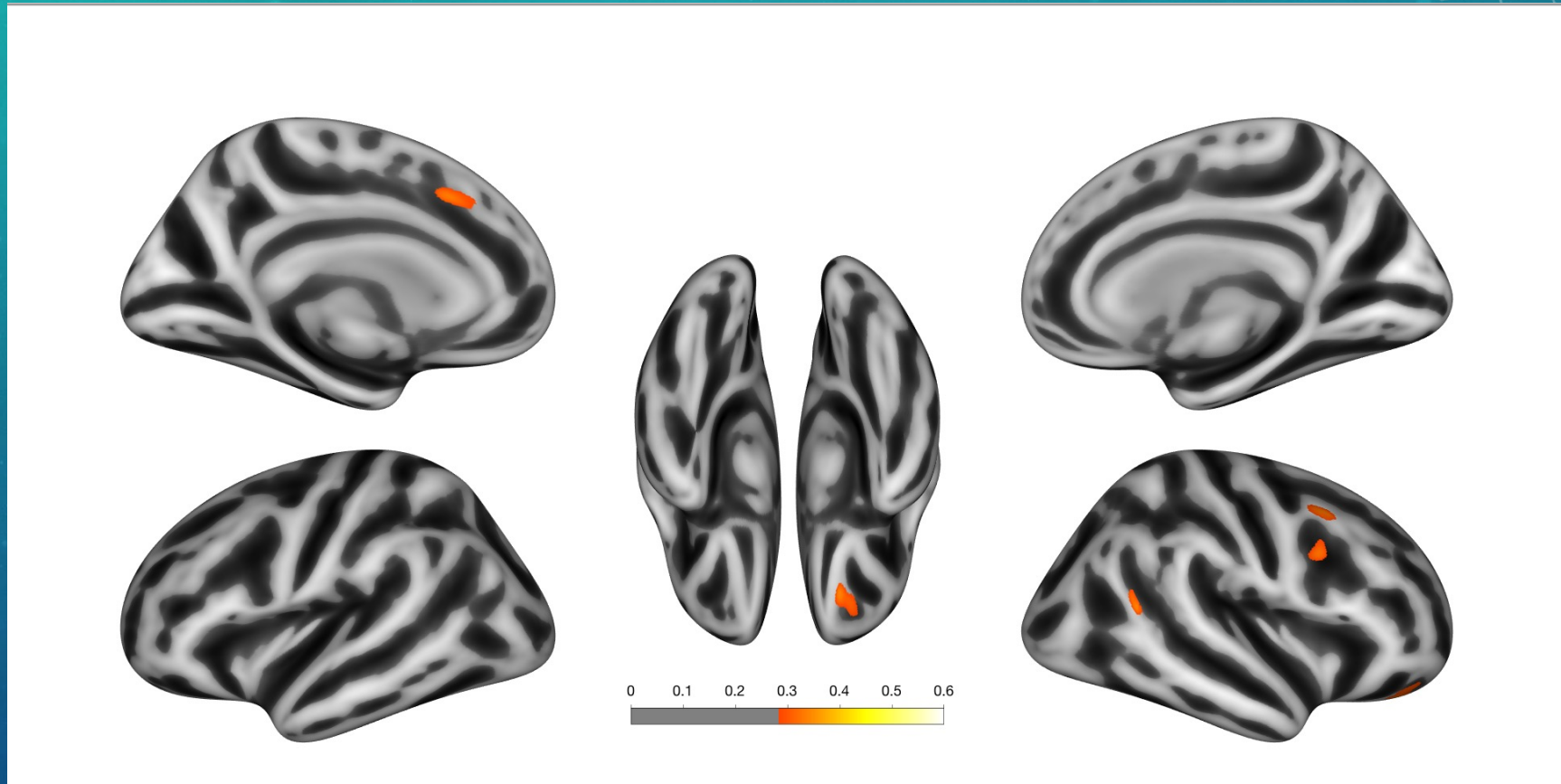


- Poorer sleep quality associated poorer white matter microstructure integrity
- Shorter sleep duration associated with smaller volumes:
 - total cerebral gray matter
 - white matter
 - hippocampus
 - thalamus

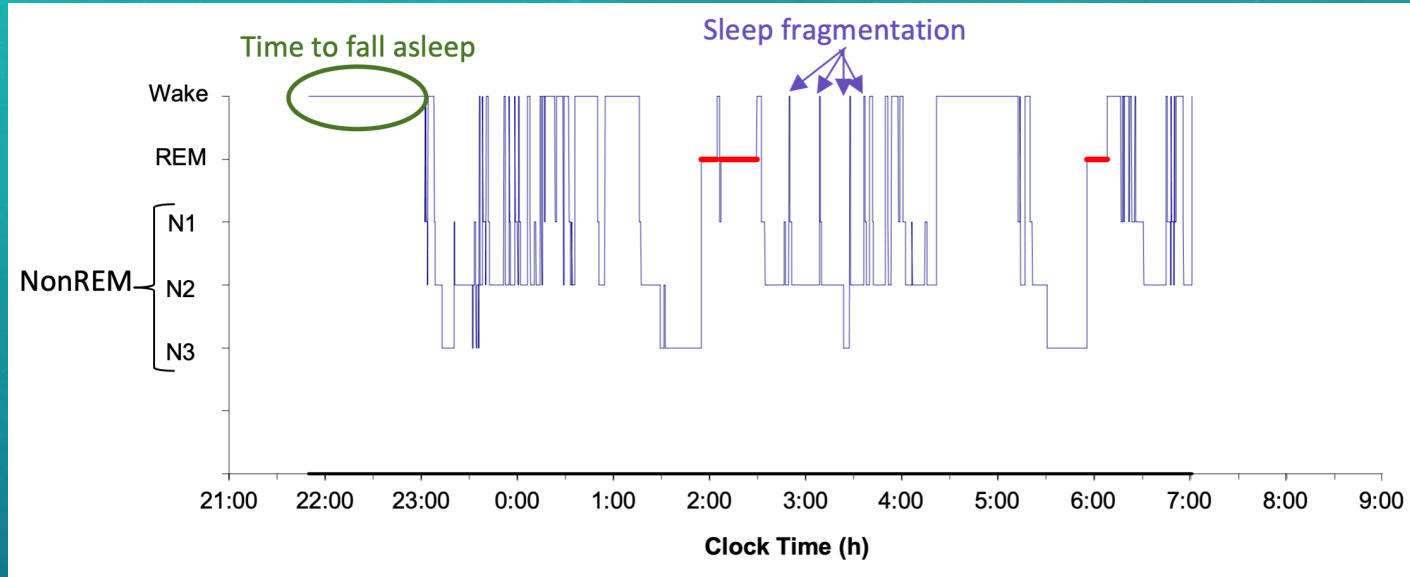


(Lo et al., 2014; Sexton et al., 2017; Liu et al., 2018; Blackwell et al., 2006 and 2011)

SUBCLINICAL INSOMNIA SEVERITY IS ASSOCIATED WITH SMALLER BRAIN VOLUMES

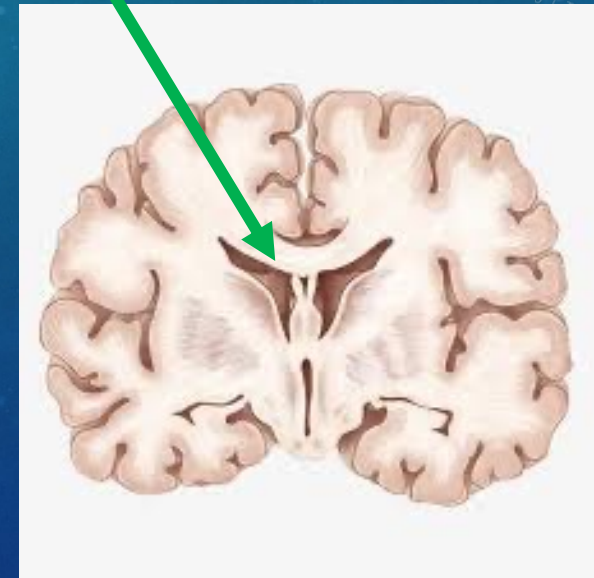
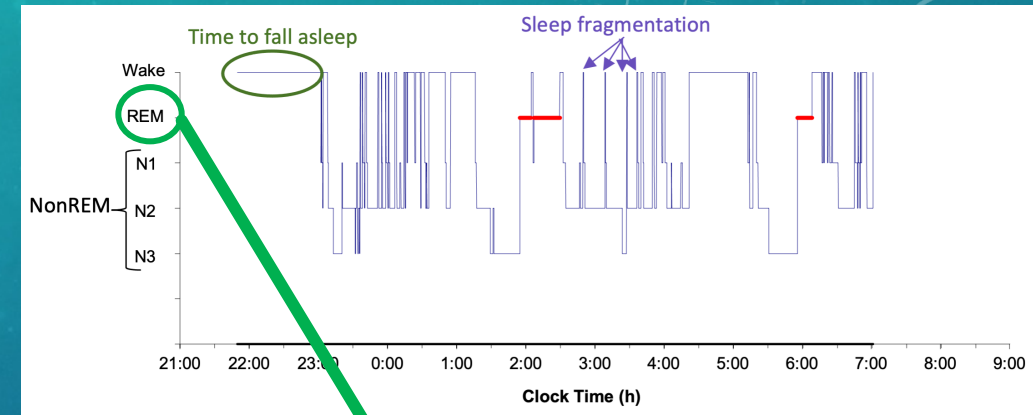
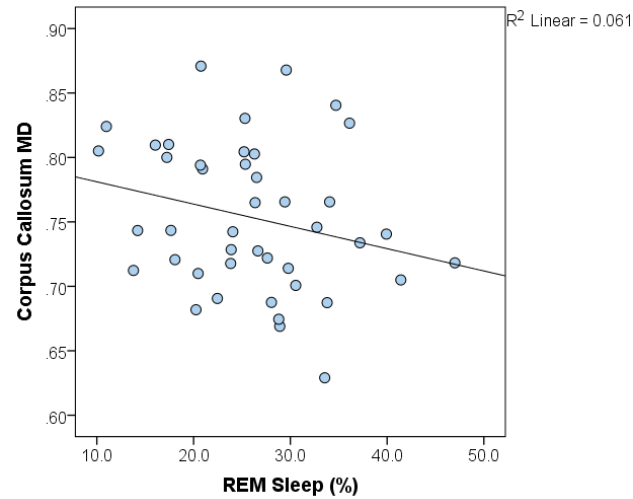
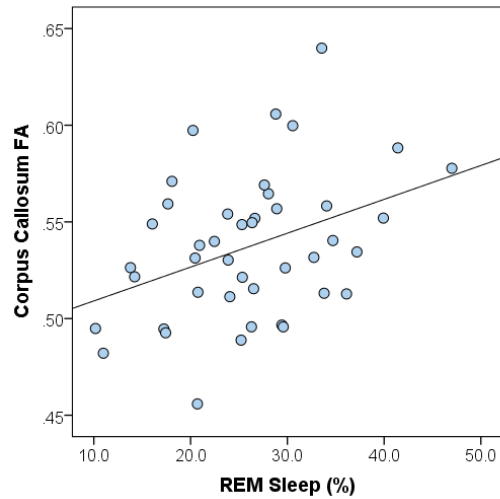


SLEEP FRAGMENTATION



- decreased grey matter volume (Lim et al., 2016)
- accounts for more than 19 percent of the variance in medial temporal lobe volumes (Van Someren et al., 2018)

REM SLEEP AND DTI OF CORPUS CALLOSUM IN HEALTHY OLDER ADULTS



A QUICK FOCUS ON REM SLEEP IN OLDER ADULTS

- Less deep sleep and REM sleep is associated with poorer cognition (memory) the subsequent day (Lafortune et al., 2014, Ye et al., 2018)
- Less REM sleep associated with steeper cognitive decline (Song et al., 2015)
- REM sleep & white matter association may be driven by:
 - blood brain permeability changes with loss of REM sleep (Gómez-González et al., 2013)
 - theta waves during REM sleep may be restorative to white matter injury (Segal et al., 2016) and support white matter health
 - Proliferation of oligodendrocyte precursor cells (OPCs) which lead to myelin production, is increased with greater REM sleep (Bellesi et al., 2013)



SLEEP CAN IMPACT COGNITIVE STATUS

Poor Sleep  Cognitive impairments (Yaffe et al., 2007; Blackwell et al., 2006, 11)

- In individuals with Mild Cognitive Impairment (MCI): longer time to fall asleep in bed was associated with impaired memory (Westerberg et al., 2010)
- Sleep disturbances **can** modulate MCI diagnosis (Gamaldo et al., 2012)



SLEEP DISORDERS AND NEURODEGENERATIVE DISEASES

HINTS INSIDE OUR SLEEP





SLEEP DISORDERS AND NEURODEGENERATIVE DISEASES

REM SLEEP BEHAVIOR DISORDER

PERIODIC LIMB MOVEMENTS

SLEEP APNEA

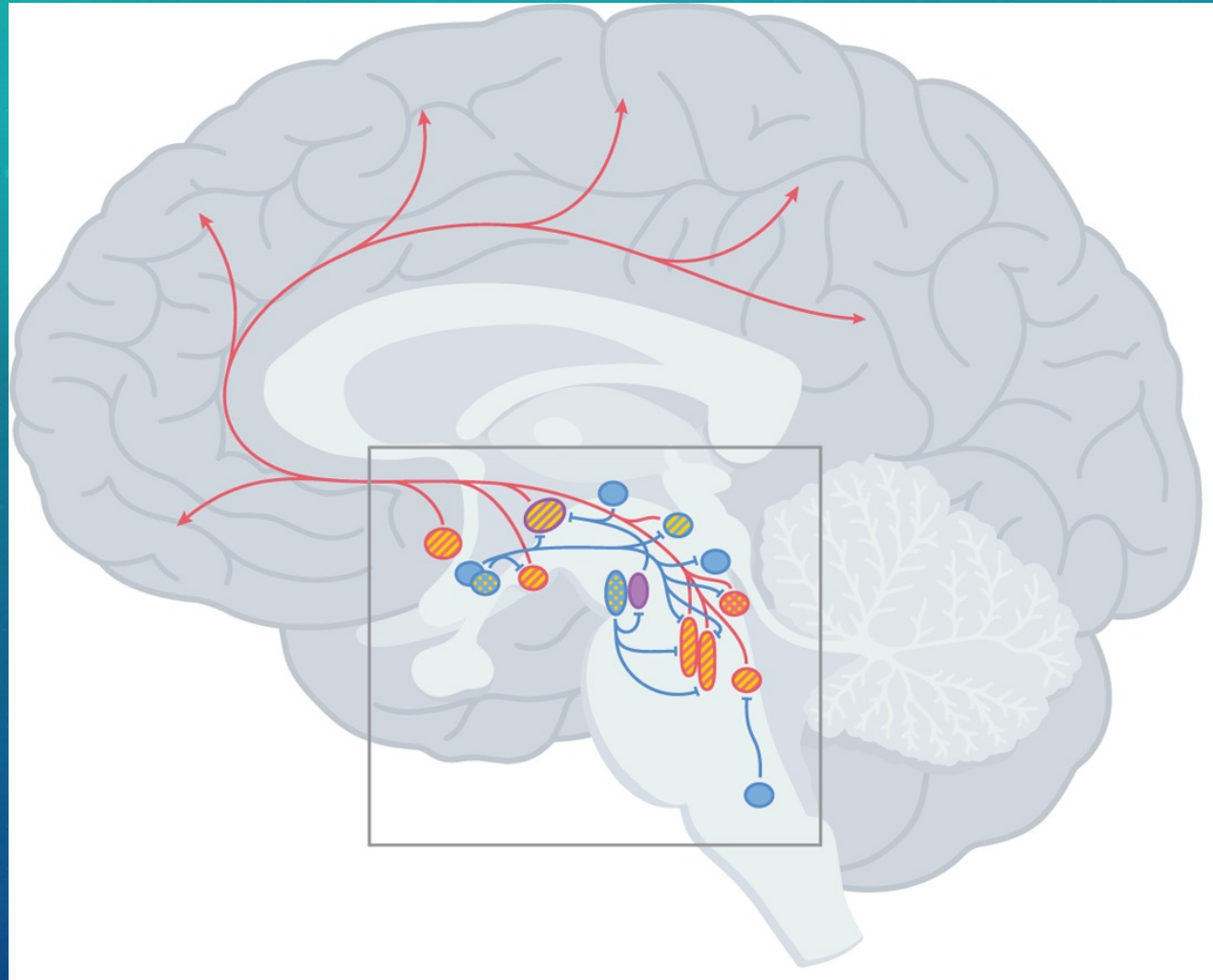
INSOMNIA



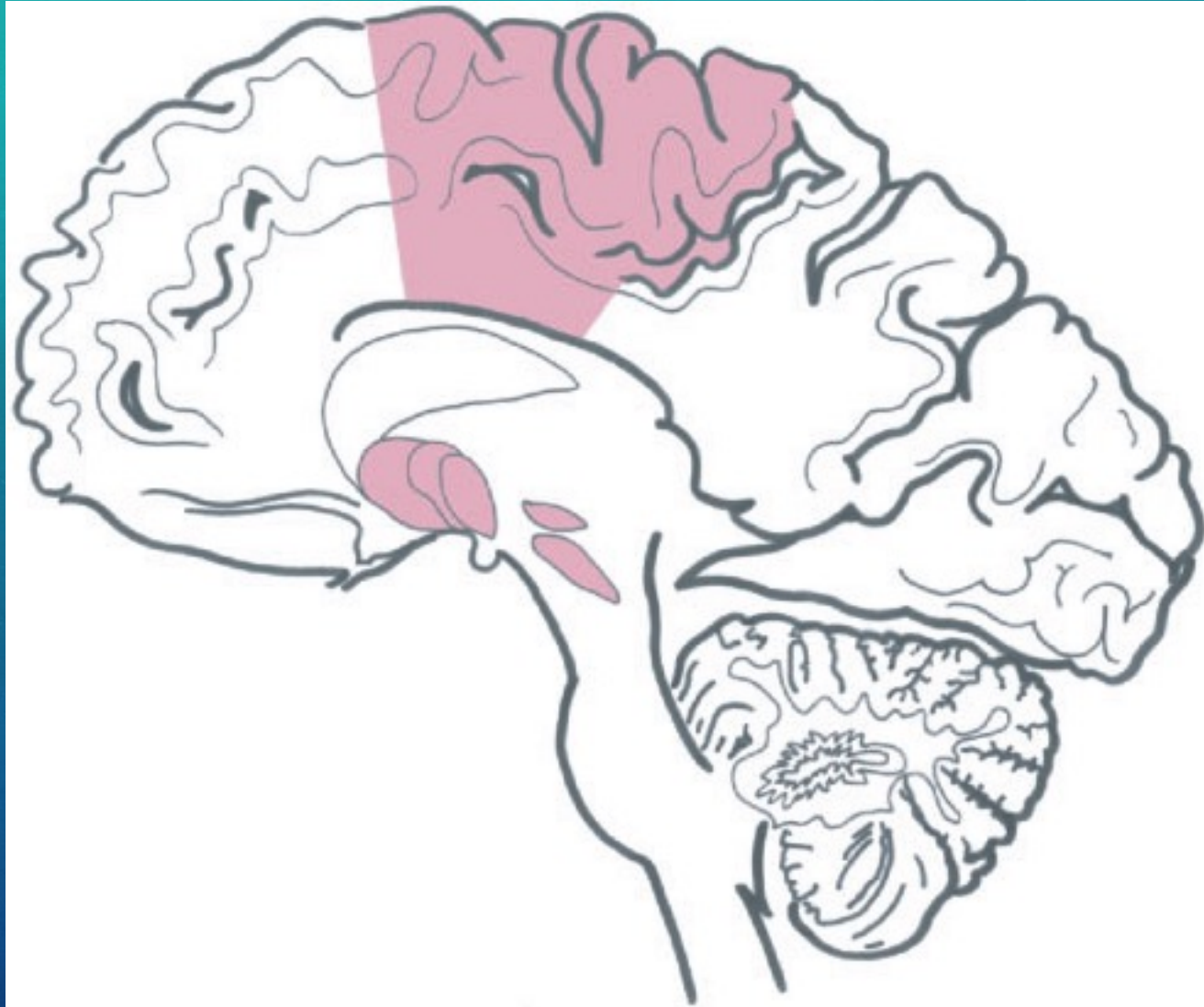
MORE DIRECT ASSOCIATION OF SLEEP AND NEURODEGENERATIVE PROCESSES

30% INCREASED RISK OF DEMENTIA IN INDIVIDUALS SLEEPING LESS THAN 6 HRS
COMPARED TO 7HRS AT 50, 60 AND 70 YEARS OF AGE (SABIA ET AL., 2021)

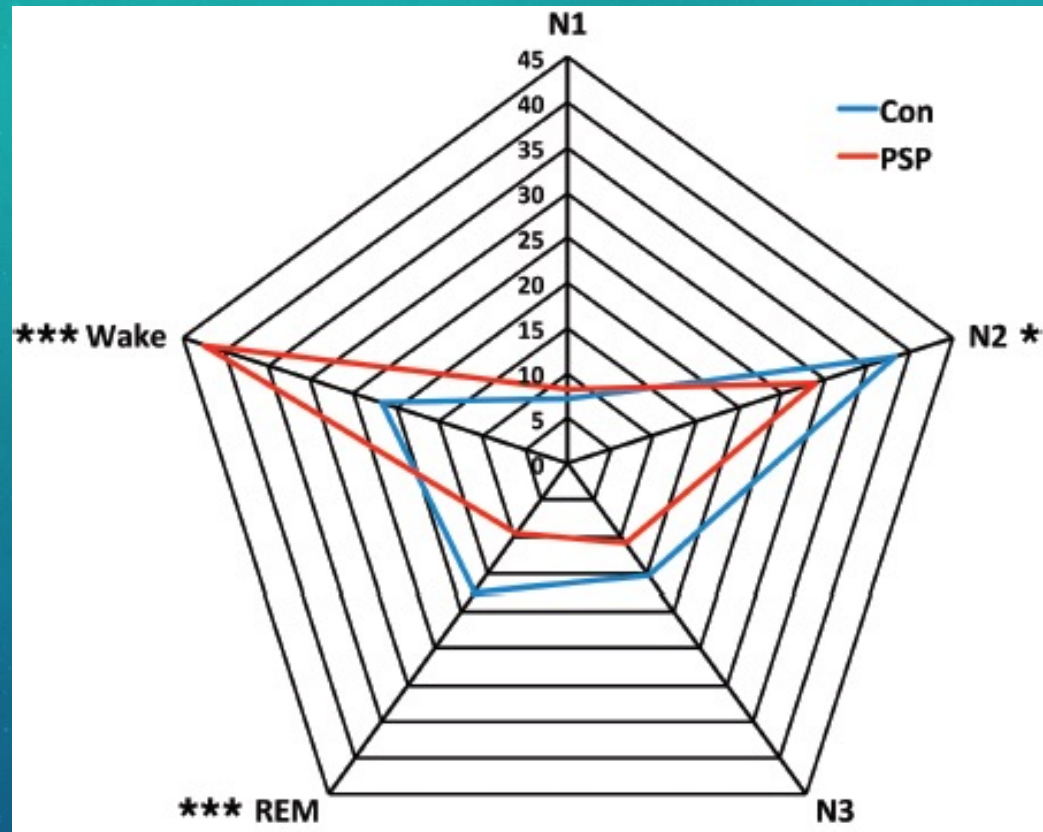
WAKE AND SLEEP PROMOTING NEURONS



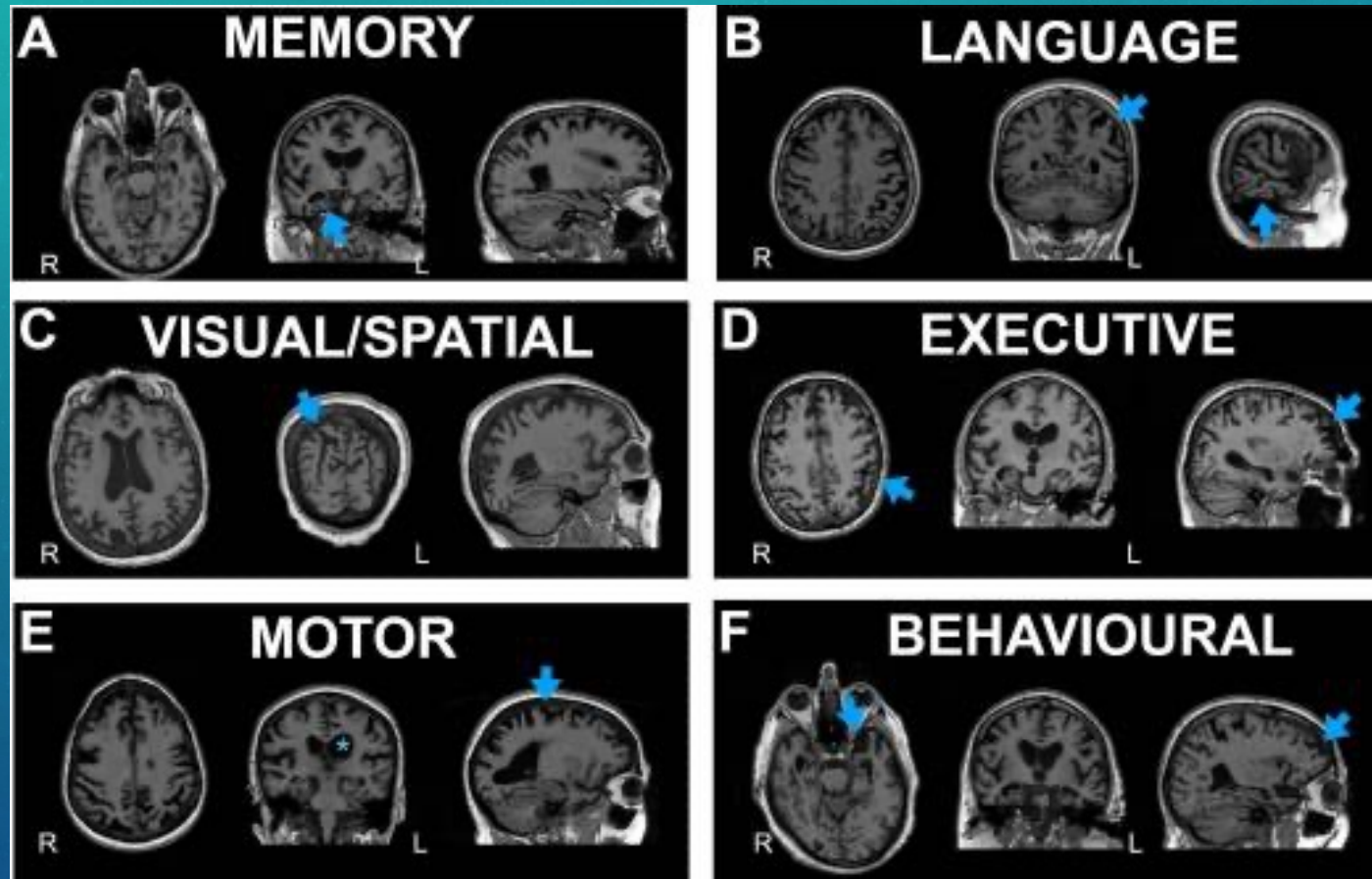
PROGRESSIVE SUPRANUCLEAR PALSY (PSP)



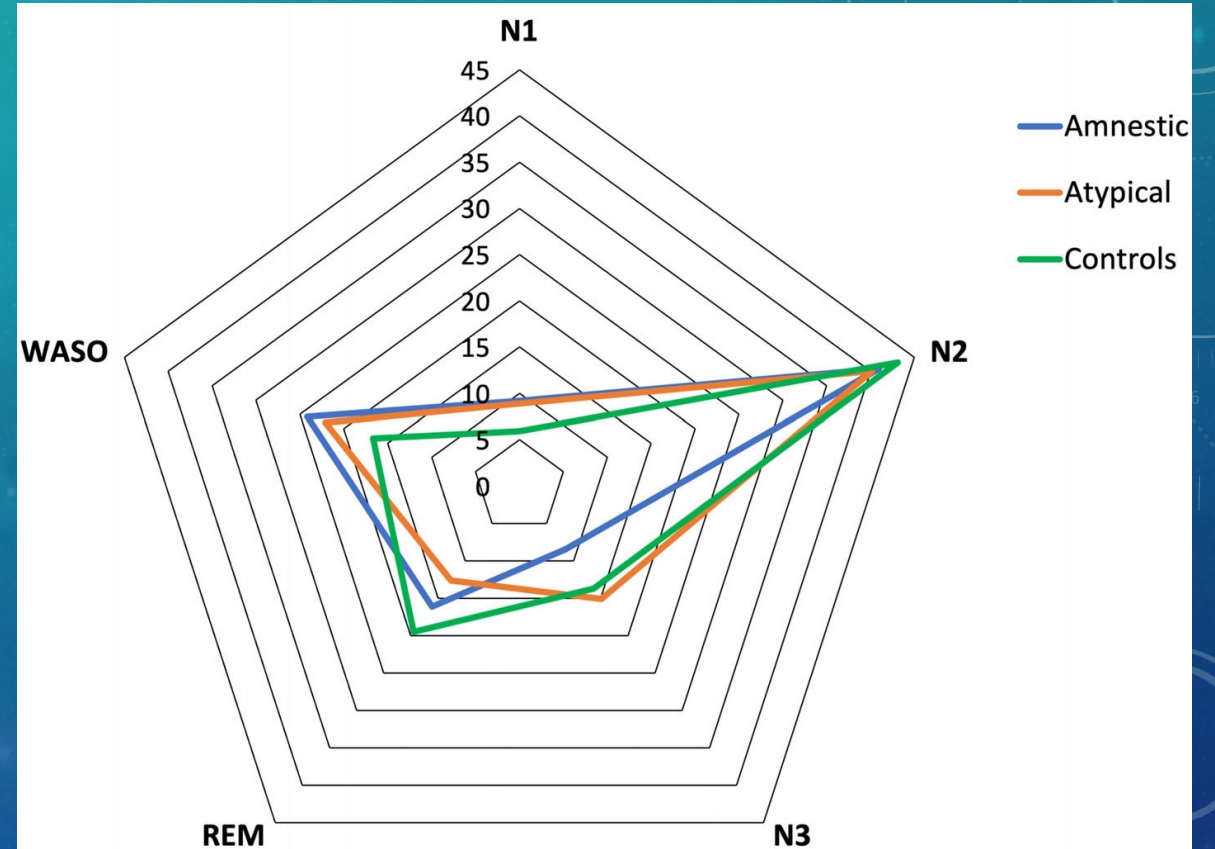
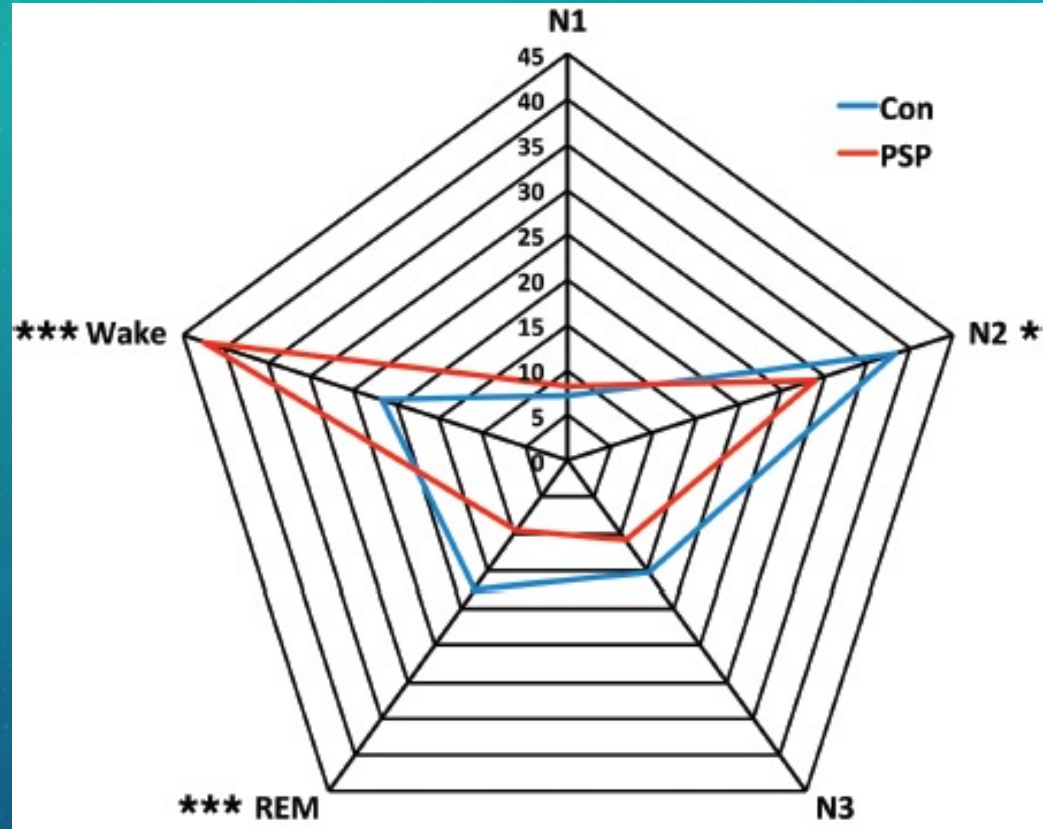
SLEEP PATTERNS ACROSS TAUOPATHIES



ALZHEIMER'S PHENOTYPE ANATOMY

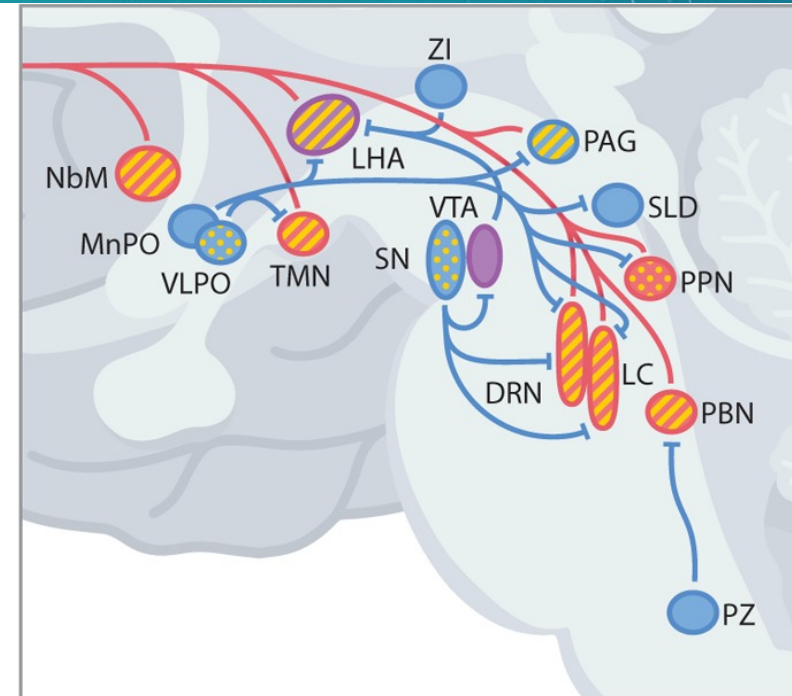
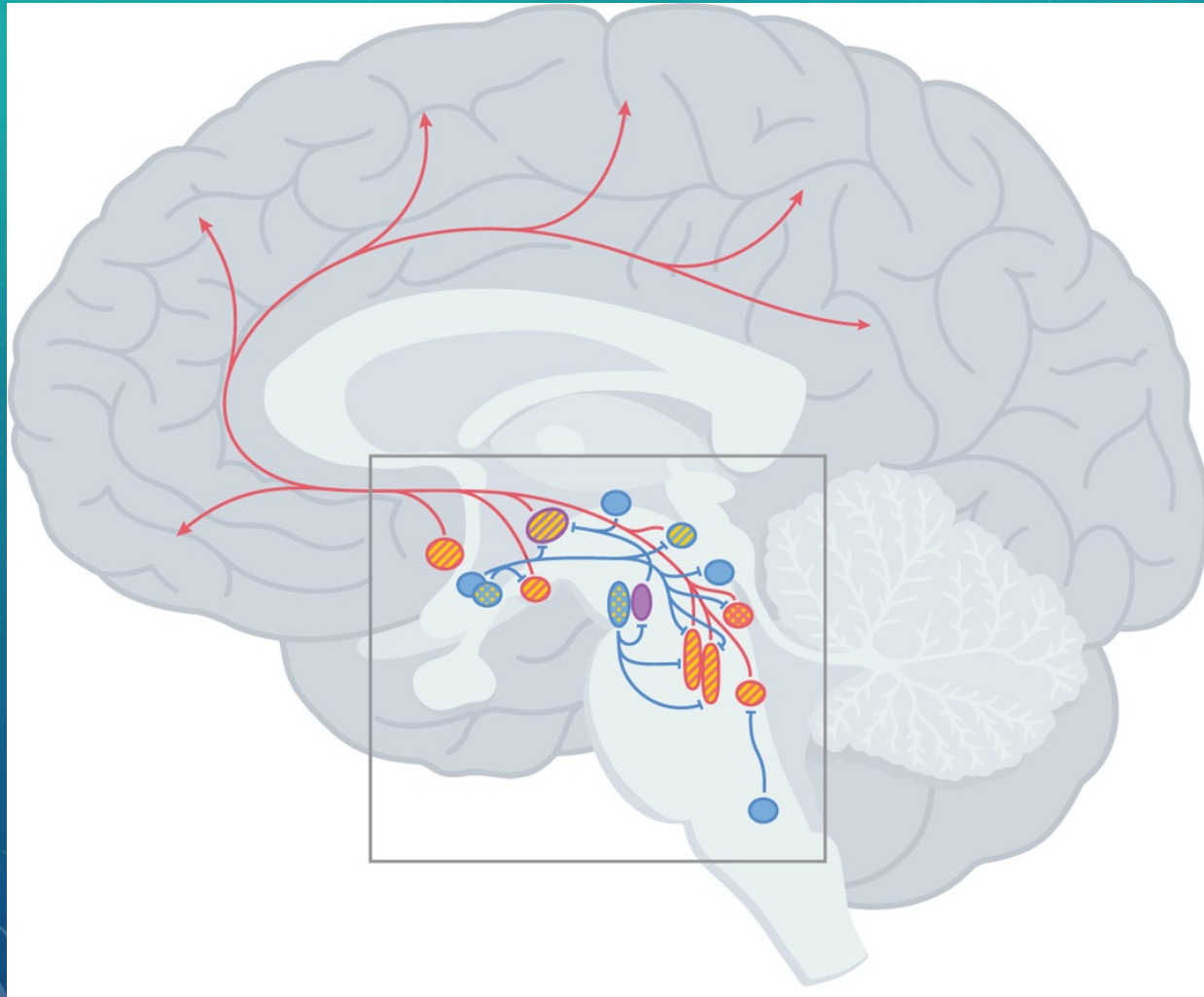


SLEEP PATTERNS ACROSS TAUOPATHIES

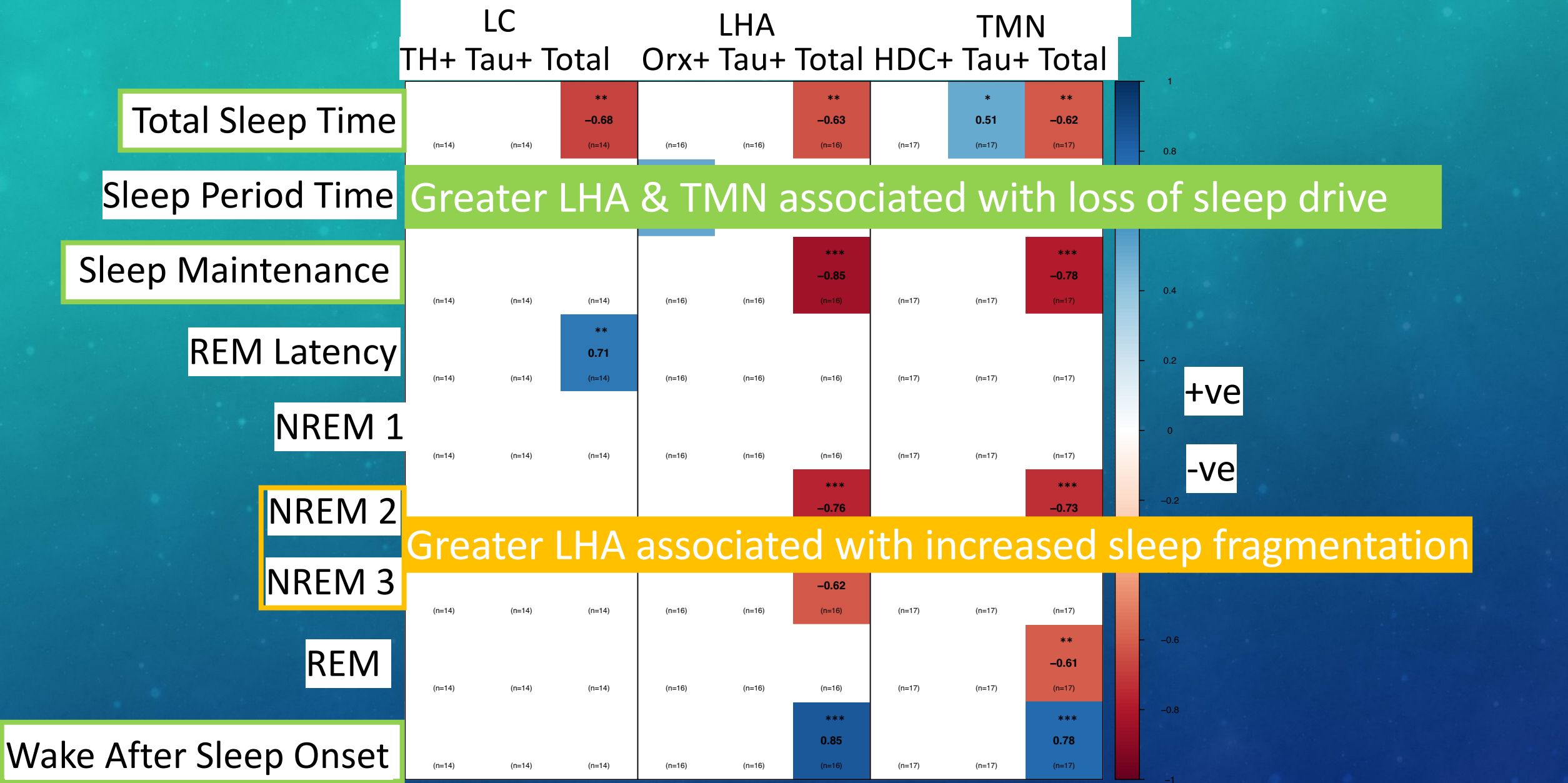


Walsh et al., 2018; Falgàs, Walsh et al, 2022

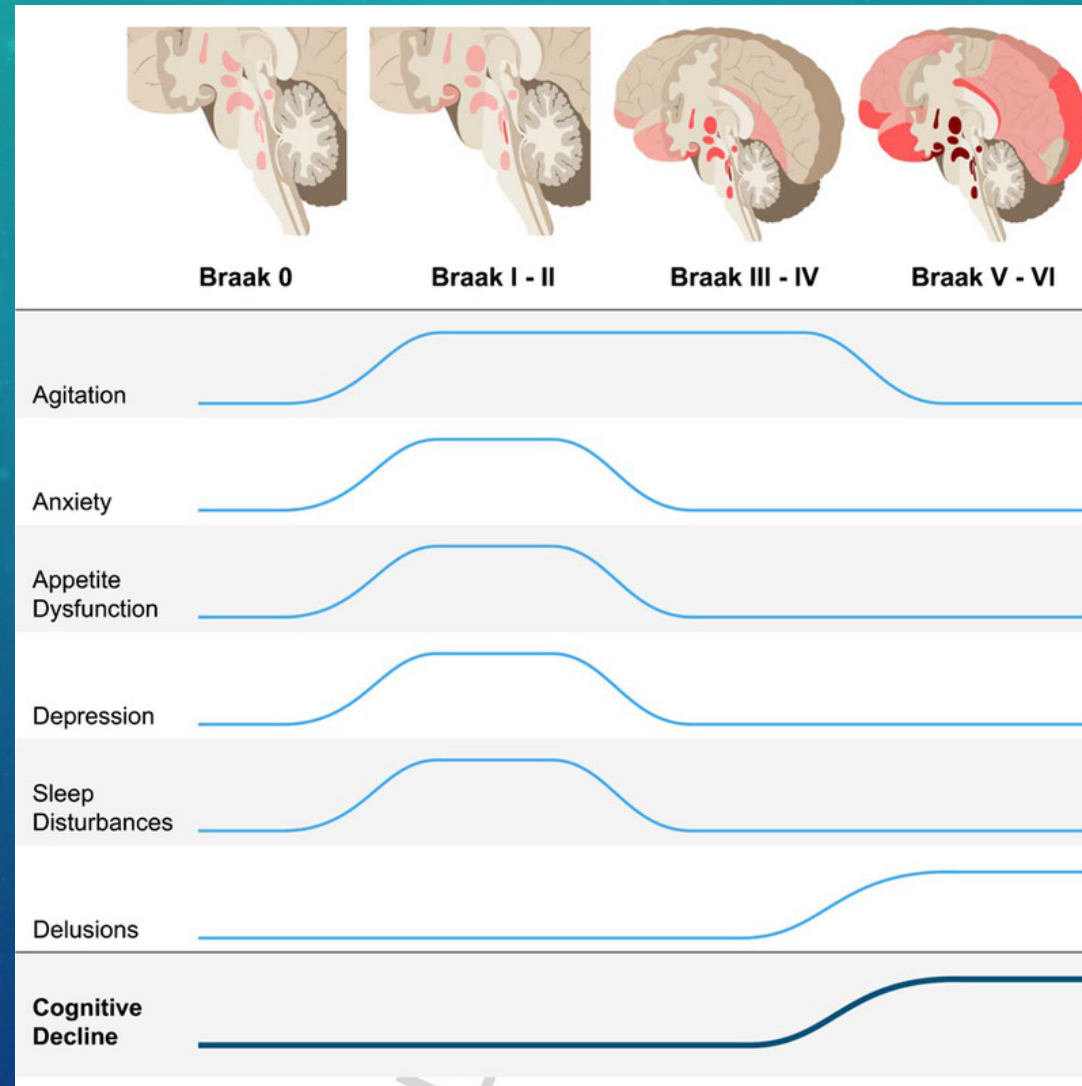
WAKE AND SLEEP PROMOTING NEURONS



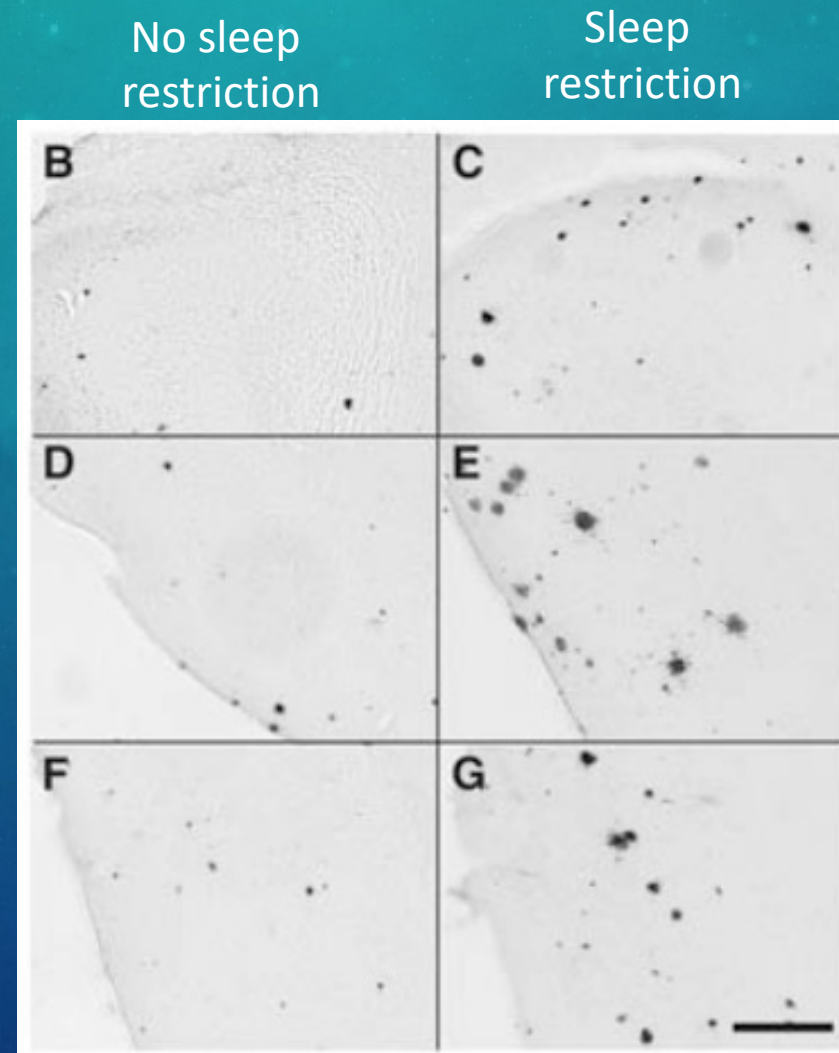
- Contains wake-promoting neurons
- Contains sleep-promoting neurons
- Contains both wake- and sleep-promoting neurons
- Tau pathology in AD Braak 0
- Tau pathology in AD reported in the literature



REPORTED SYMPTOMS & TAU PATHOLOGY IN ALZHEIMER'S DISEASE



AMYLOID PLAQUE DEPOSITS INCREASE WITH REDUCED AMOUNTS OF SLEEP IN MICE

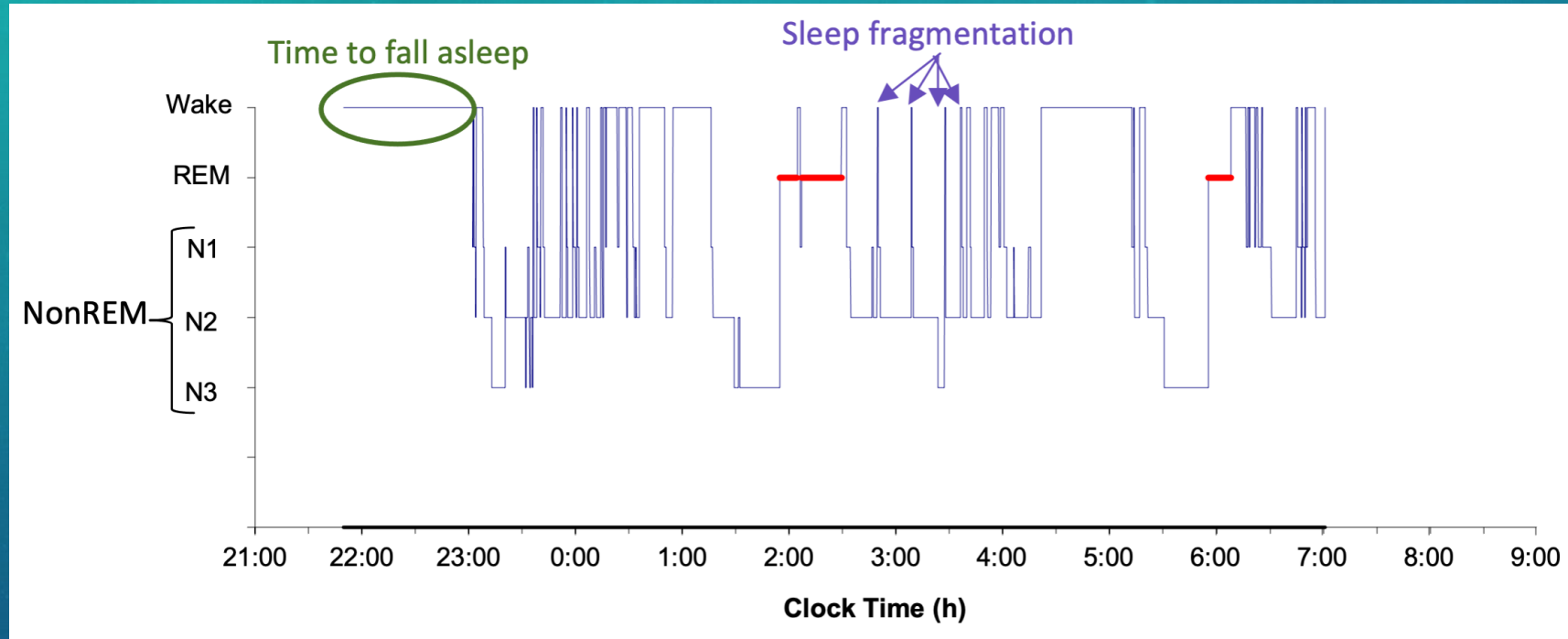


Olfactory Bulb

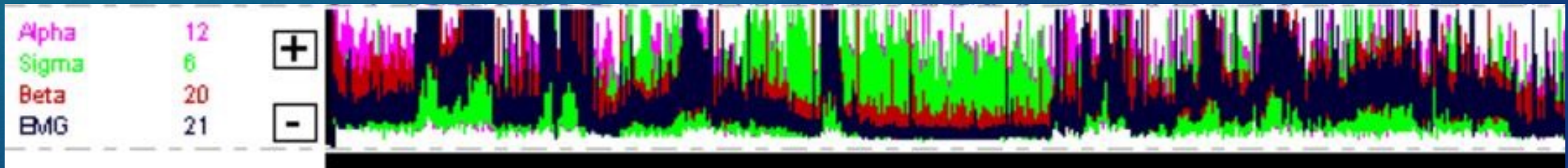
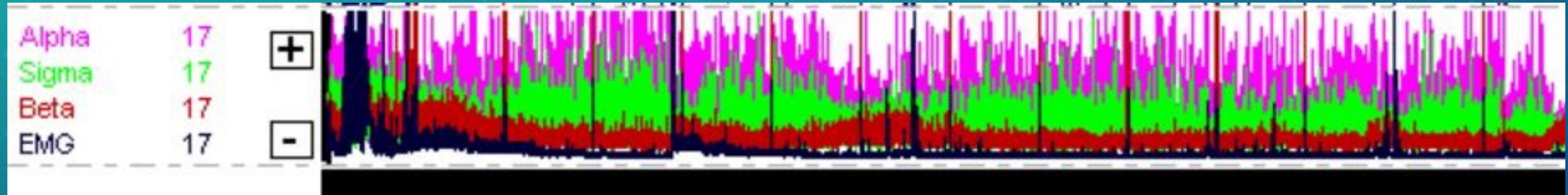
Piriform Cortex

Entorhinal Cortex

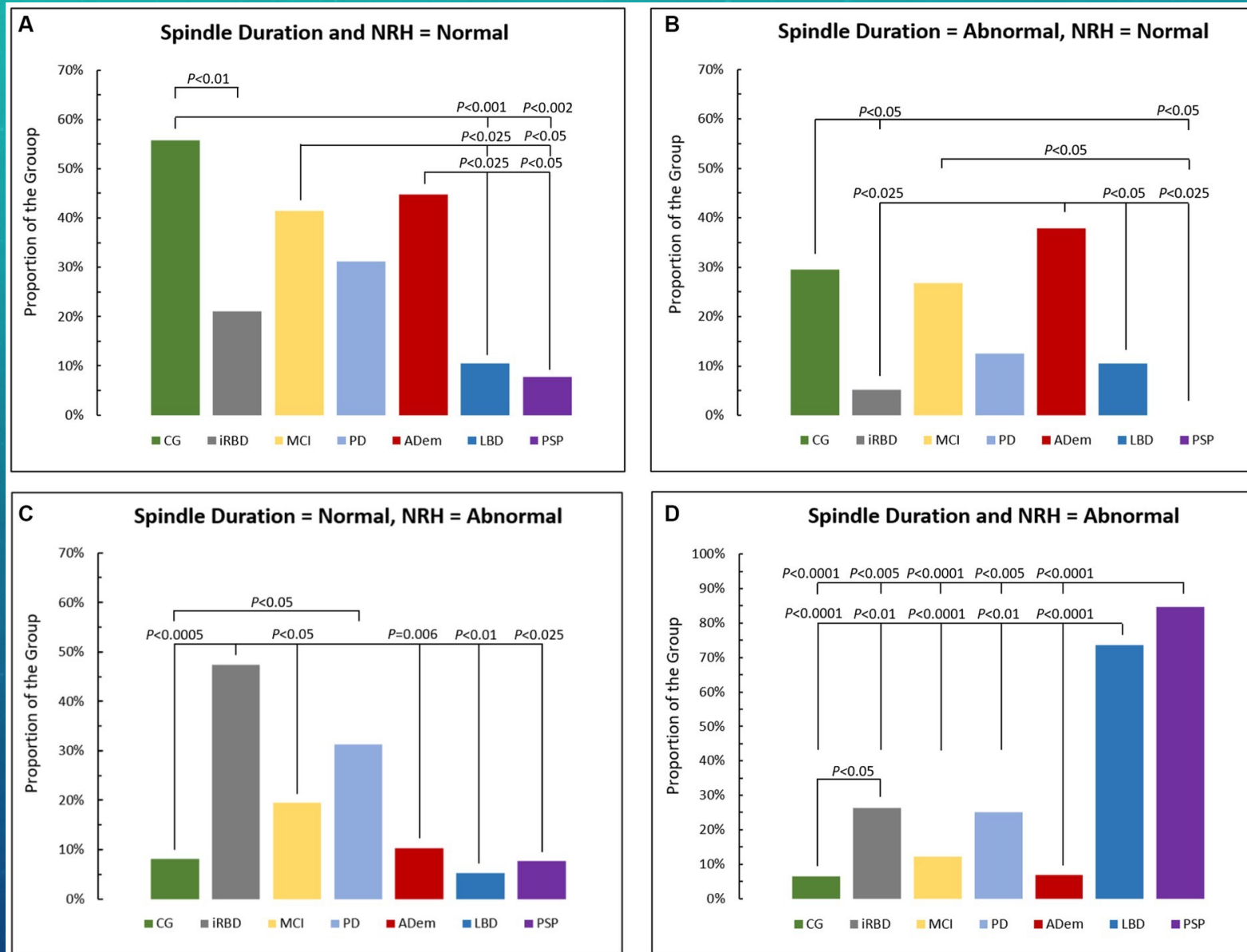
UNDERSTANDING SLEEP BEYOND SLEEP STAGES

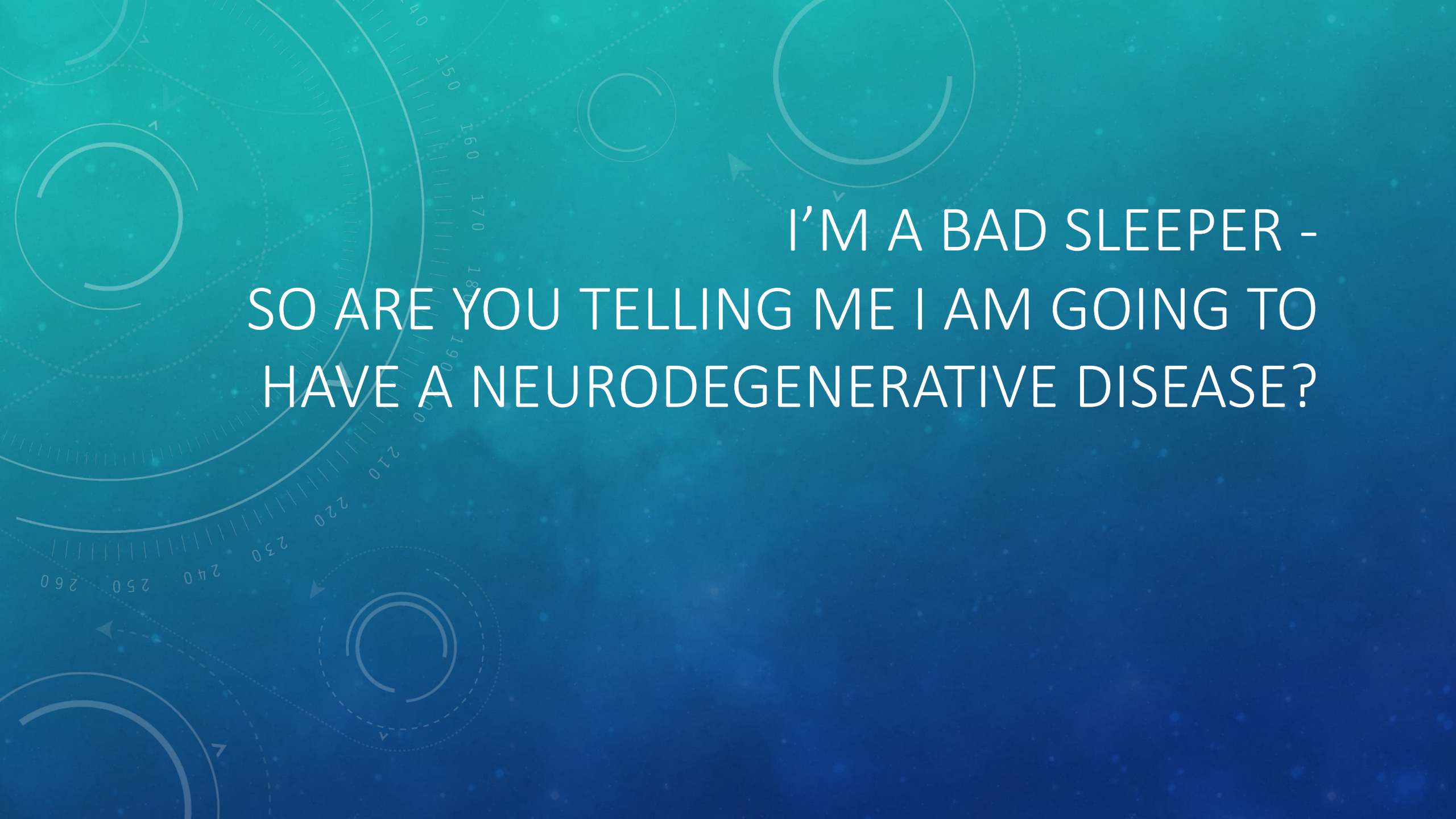


MULTI-SITE STUDY: NONREM SLEEP HYPERTONIA



DIFFERING SLEEP PATTERNS





I'M A BAD SLEEPER -
SO ARE YOU TELLING ME I AM GOING TO
HAVE A NEURODEGENERATIVE DISEASE?

HINTS INSIDE OUR SLEEP



TREATABLE FACTORS THAT COULD IMPROVE SLEEP

- Hypertension increases sleep disruption (Eshkoor et al., 2013)
- Ischemic heart disease, diabetes, depression, arthritis and pulmonary disorders increase insomnia (Deschenes & McCurry, 2009)
- Ischemic heart disease, congestive heart failure and cardiomyopathy increase obstructive sleep apnea and restless leg syndrome (Deschenes & McCurry, 2009)
 - but diuretics increase sleep disruption
- Increased pain increases insomnia
 - but treatments can increase excessive daytime sleepiness

GOOD SLEEP HYGIENE

- Maintain regular bedtime and rise-time throughout the week
- Limit time in bed to sleeping
- Avoid or reduce napping
- Exercise before 2pm
- Spend time in natural light
- Avoid caffeine, nicotine and alcohol close to bedtime
- Establish a comfortable sleep environment
- Establish a calming nighttime routine

SUGGESTIONS FOR IMPROVING SLEEP THROUGH MODIFIED BEHAVIORS

- Environment
 - Bedroom
 - Quiet and consistently familiar
 - Keep the room as dark as possible
 - Reduce potential sleep interruptions (noise, pets, comfortable temperature)
 - Morning exposure to sunlight or bright light

SUGGESTIONS FOR IMPROVING SLEEP THROUGH MODIFIED BEHAVIORS

- Eating & Activities
 - Consistent mealtimes
 - Avoid alcohol, nicotine and caffeine
 - Void the bladder before bedtime
 - Limit fluid intake prior to bedtime
 - Routine daily activities
 - Avoid too many activities near bedtime

BE SOCIAL TO SLEEP

- During the pandemic, individuals who reported greater social participation and a sense of belonging had better subjective sleep quality (Xiao et al., 2020)
- Trying to not feel lonely, may improve sleep quality (Altena et al., 2020)
- Being social diminishes stress (Devries et al., 2003) and improves sleep (De Grey et al., 2018)

IMPROVING SLEEP, COGNITION AND LOWERING STRESS THROUGH MEDITATION

- In collaboration with Neuroscape, UCSF
- Meditation training program with brain imaging and at-home sleep assessments
- Cognitively healthy older adults and individuals with Mild Cognitive Impairment (MCI)
- Christine.walsh@ucsf.edu or meditrain@ucsf.edu (include MediDream in the subject line)

CAREGIVING THROUGH THE NIGHT

- Caregivers have lower sleep durations (~ 2.4 – 3.5hrs less / week; Gao et al., 2019)
- Sleep helps mood and emotions
 - reduce stress / anxiety
 - can reduce depression
 - helps regulate emotions
 - helps in reading emotions
 - helps in risk-assessment
 - helps in judgement and negotiating
- Sleep helps overall health
 - the immune system
 - insulin / ghrelin regulation
 - neural health

HOW CAN A CAREGIVER SLEEP?

- The “Try Tos”
 - reduce likelihood of un-checked sleep disorders for you and your loved-one
 - (also talk to dr about medication schedule)
 - maintain a stable sleep pattern (bedtime and final rise time)
 - exercise or get some daylight in the morning
 - reduce your level of alertness during the night
 - use a patient bed monitor or door monitor
 - or set an alarm if needed for night time care
 - follow general sleep hygiene guidelines as best you can
 - continue being social, including attending groups like this

PATIENT / CARE PARTNER INTERVENTION STUDY

- Developing Strategies to Manage Poor Sleep Among Persons Living with Dementia and Their Family Caregivers
- Remote study over zoom
- Yeonsu Song, PhD, RN, FNP
- ysong@sonnet.ucla.edu

TIPS FOR SLEEPING YOUR WAY TO A HEALTHIER YOU

- Try to maintain stable sleep patterns
- Follow a healthy sleep hygiene program
- Exercise in the day before the evening
- Get exposure to sunlight/ bright light in the morning
- Communicate with family / friends
- Avoid napping in the late afternoon / evening
- Limit caffeine and alcohol
- Mediterranean diet may help (Mamalaki et al., 2018)
- Try not to become too preoccupied with how much sleep you are getting

THANK YOU

Christine.walsh@ucsf.edu

UCSF Weill Institute for Neurosciences
Memory and Aging Center



RESOURCES

National Institutes of Health

[http://www.nhlbi.nih.gov/health/public/sleep/healthy_sleep.p
df](http://www.nhlbi.nih.gov/health/public/sleep/healthy_sleep.pdf)

NATIONAL SLEEP FOUNDATION

www.sleepfoundation.org