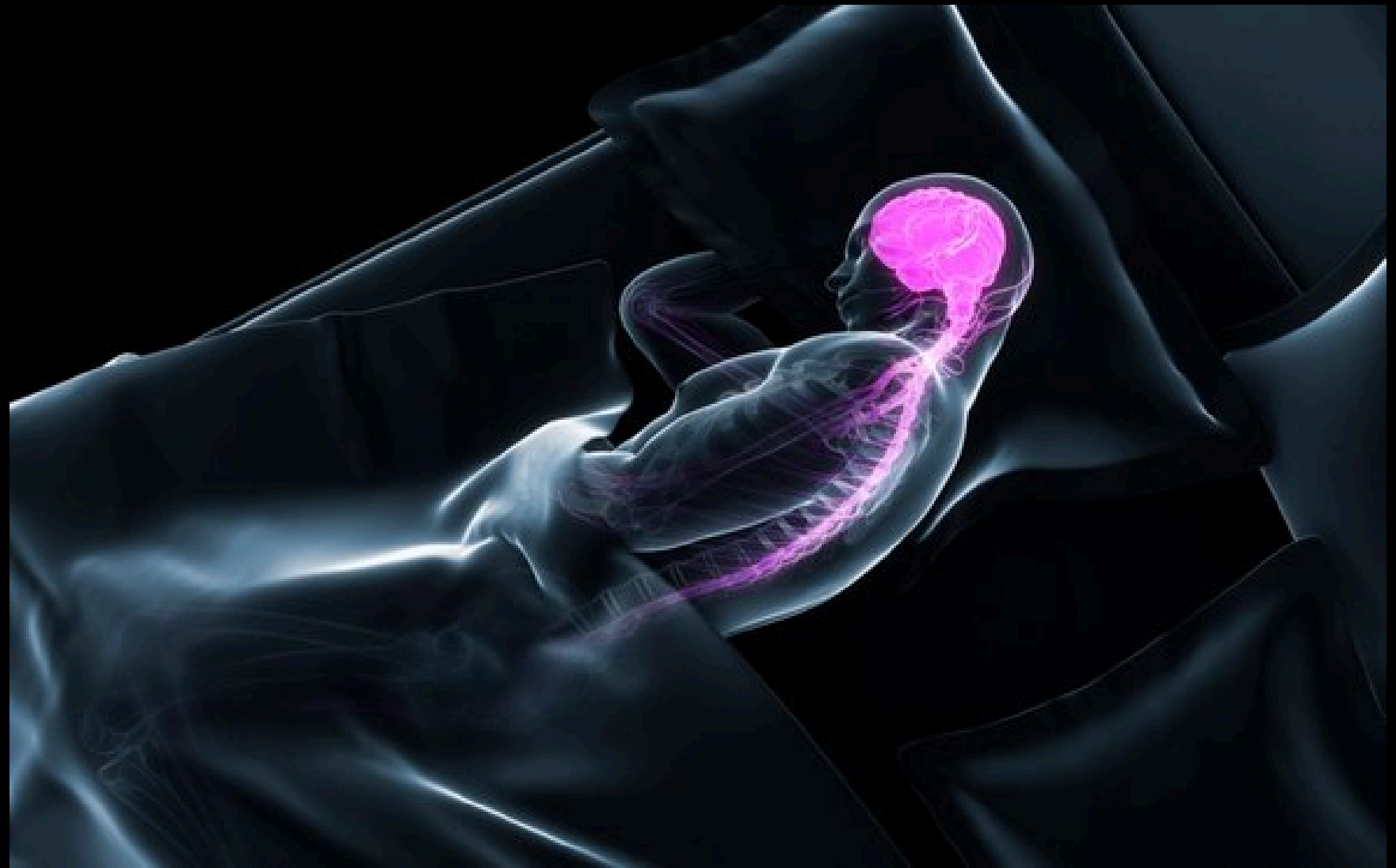
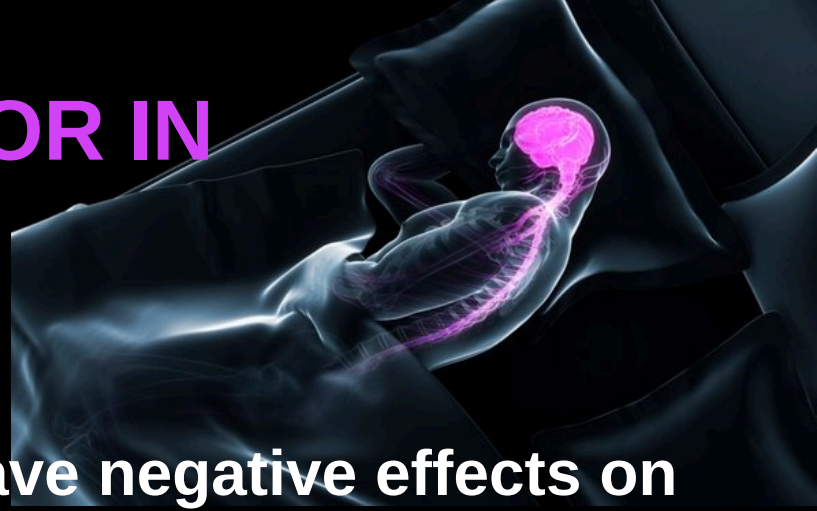
SLEEP AFFECTS HOW WELL BRAIN RESISTS COGNITIVE DECLINE & DEMENTIA



SLEEP: KEY MODIFIABLE RISK FACTOR IN SLOWING & PREVENTING COGNITIVE DECLINE & DEMENTIA

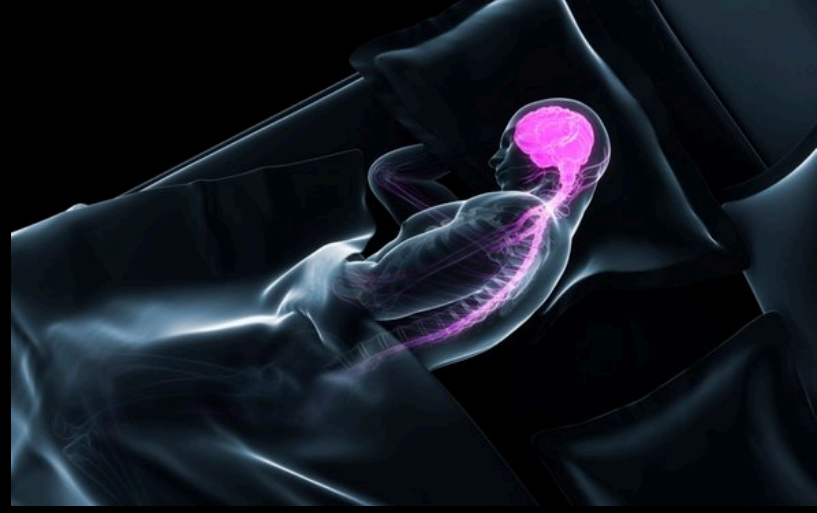


- **Chronic sleep disturbances, particularly SDB, can have negative effects on cognitive function and increase risk of cognitive decline and impairment – including MCI and AD** (Yaffe 2014, Blackwell 2011)
  - Performance on cognitive tests is lower for community-dwelling older adults with SDB than for those without the disorder – particularly for executive function (Ancoli-Israel 1991)
  - In older women (n=448; mean age=83y), SDB predicted low global cognitive function (MMSE) (Spira, Redline 2008)
  - Study of Osteoporotic Fractures (mean age=82y) with >4 years of follow-up after overnight polysomnography, hypoxemic events/hour and total hypoxemic sleep time predicted later onset of MCI or dementia (Yaffe 2011)
  - In a large population-based retrospective study, diagnosed sleep apnea was associated with increased risk of dementia within 5 years (Chang 2013)

SLEEP: KEY MODIFIABLE RISK FACTOR IN SLOWING & PREVENTING COGNITIVE DECLINE & DEMENTIA

- Kungsholmen Study: Self-reported short sleep duration or poor sleep quality predicted increased risk of dementia assessed 6-9 years later (Hahn 2014)
- Rush Memory and Aging Project: Sleep fragmentation predicted increased rate of cognitive decline and incident AD assessed up to 6 years later (Lim 2013)
- WHI: Similar findings in a small study (Chen et al. 2015)

SLEEP & COGNITIVE FUNCTION: UNDERLYING MECHANISMS



Sleep

Oxidative Stress

Sleep

Glucose Regulation

Sleep

Inflammation

Metabolic Syndrome

Sleep

Sleep

Hypertension

Cognitive Function

Neuropathology (atrophy, plaques & tangles)

Sleep

Sleep

Silent Strokes

Endothelial Dysfunction

WM Damage

Sleep

Sleep

SLEEP & AD PREVENTION: IMPACT ON NEUROPATHOLOGY

- Declines in sleep quality appear to precede cognitive impairment, and chronic sleep disturbance forecasts development of AD (Ju 2014)

  - o Poorer sleep quality in non-demented older adults associated with lower Aβ concentration in cerebrospinal fluid, or increased Aβ binding in brain measured using PET imaging – signify increased deposition and increased AD risk (Ju 2013, Spira, Resnick 2013)

    - Unrestricted sleep → favorable effects on Aβ levels in CSF of middle aged adults, 1 night of sleep deprivation can neutralize this benefit (Ooms 2014)

  - o Better sleep quality (less sleep fragmentation) protects against ApoE4 effects on AD-related cognitive decline and neuropathological changes (Lim 2013)

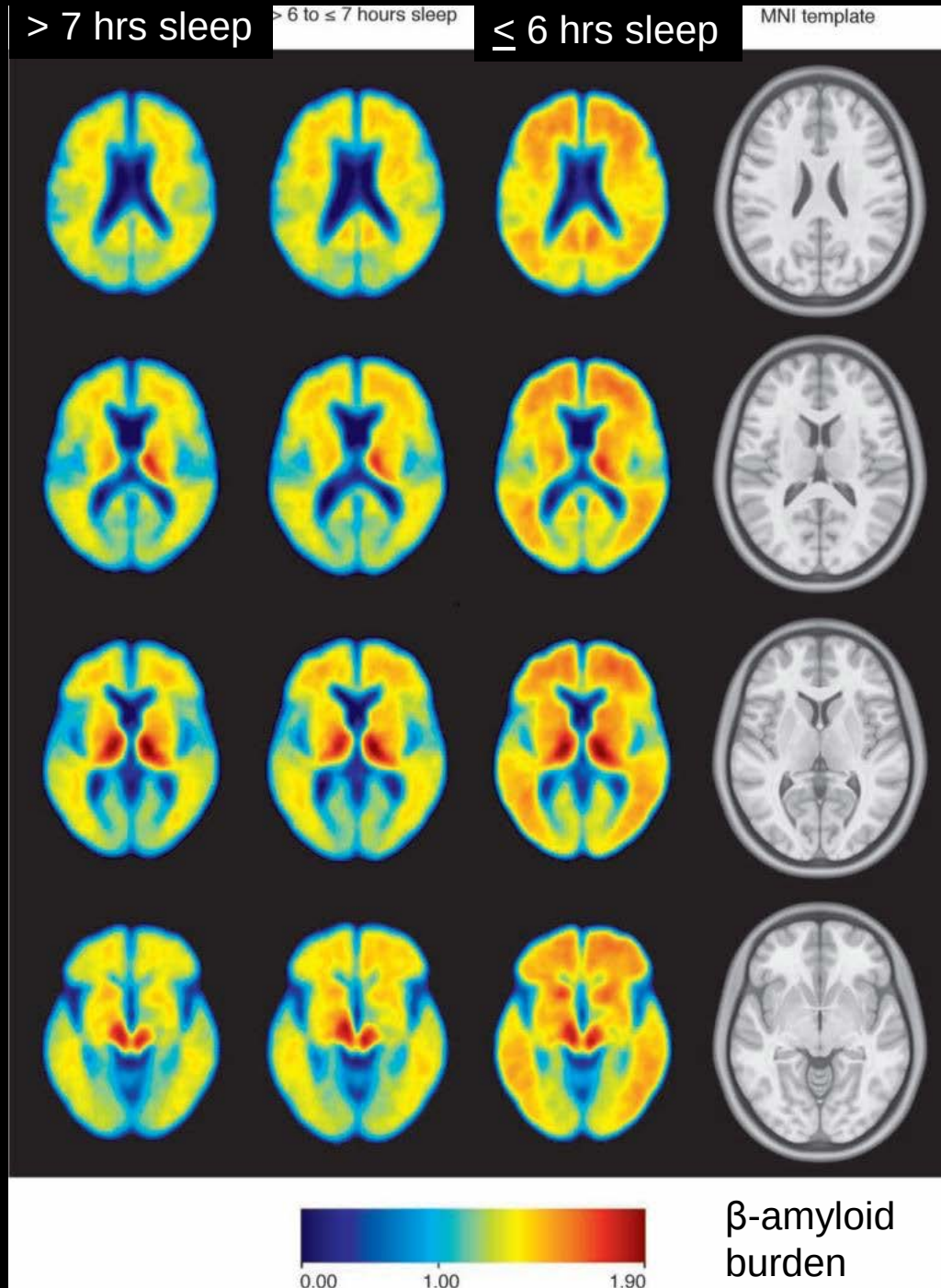
SLEEP & AD PREVENTION: IMPACT ON NEUROPATHOLOGY

- **Midlife sleep quality by self-report (short or x-long sleep duration) predicted cognitive function 20+ years later**
  (Virta et al. 2013)

- **Sleep may be critical for Aβ clearance from the brain**
  (Xie 2013)

Spira, Resnick, 2013; Baltimore Longitudinal Study of Aging;

4 axial slices showing more burden with less sleep by self-report in 70 older adults



IMPLICATIONS FOR WHI

- Scope of the problem in older women?
- Impact on women's health over the long run?
- Implications for healthcare down the road?
  - Detection of abnormalities?
  - Therapeutics?
- Next steps in WHI?
  - Collaborations?
  - Indications?
  - Clinical trials?