CHRONIC SLEEP LOSS: NEURODEGENERATION

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SIGNIFICANCE: WE PUSH THE SYSTEM

Majority of adolescents do not get adequate sleep.
40% of adults do not get 7-8 hrs sleep.
3% have nodded off driving...in the past month.

RECHTSCHAFFEN STUDIES:
Rats died of sleep deprivation but with minimal brain injury.
SIGNIFICANCE: CAN CHRONIC SLEEP LOSS AGE THE BRAIN AND MODULATE NEURODEGENERATION?

• Retired shift workers:
  – Increased complaints of poor sleep and wakefulness

• Sleep and amyloid interactions (Holtzman, Nedergaard, Tabuchi)
  – Collectively suggest vicious cycle

• Sleep loss and brain oxidative and ER stress:
  – Can sleep loss accelerate aging of the brain
  – By aging the brain can sleep loss shift onset of Alzheimer’s?
STATE OF THE ART (SOTA) IN HUMANS: DELAYED/INCOMPLETE RECOVERY OF ALERTNESS

Belenky et al., J Sleep Research 2003;12:1-12
Extended wakefulness:
Locus coeruleus oxidative stress, mitochondrial injury & degeneration

Zhang et al., 2014 J Neurosci
CHRONIC INTERMITTENT SLEEP LOSS
MODELING SHIFT WORK

Chronic short sleep 4 hr less/24hr period
STATE OF THE ART RECOVERY
LOSS OF LOCUS COERULEUS NEURONS
LC LOSS: DEPRESSION AND ALZHEIMER’S PROGRESSION
KNOWLEDGE GAPS: THE SWITCH

Locus coeruleus neuron

Ca++

isradapine
CAV1.3 channel
SERCA
Endoplasmic reticulum
Ryanodine
MCU
RU360
MCU-/- mice
Mitochondrion
NOS>NO>ETC O2
SirT3
NAD+

Calcium overload
Mitochondrial compromise
Impaired axonal transport
Disrupted autophagy
MOVING FORWARD: WHAT IS NEEDED TO ADVANCE THE AREA

- Is injury from sleep loss confined to wake-neurons or also injurious to sleep-active neurons?
- What is irreversible?
- What is the extent of injury?
- How does this neural injury impact peripheral systems/health?
- Do these changes represent accelerated aging?
- What mechanisms dictate the injury and what responses modulate the severity of response?
- Can we reverse age-related changes and chronic sleep loss related changes?
- How does this injury influence Alzheimer’s disease and other neurodegenerative processes?