



CHRONIC SLEEP LOSS: NEURODEGENERATION

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DISCLOSURES/CONFLICTS OF INTEREST

- Current funding: NIH HLBI
- Other financial relationships: none
- Conflicts of interest: none

SIGNIFICANCE: WE PUSH THE SYSTEM



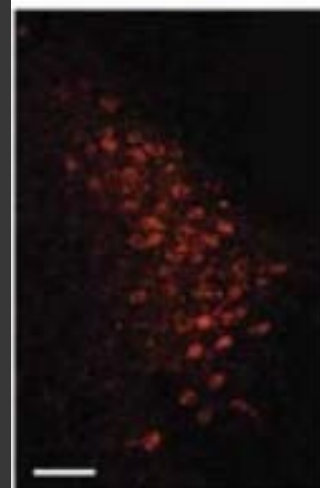
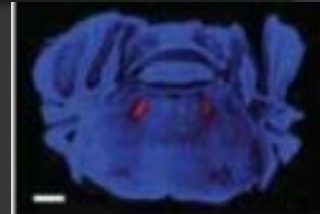
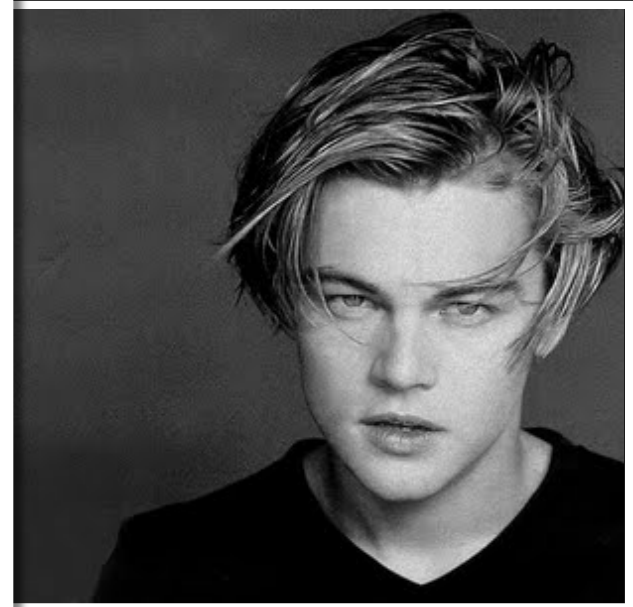
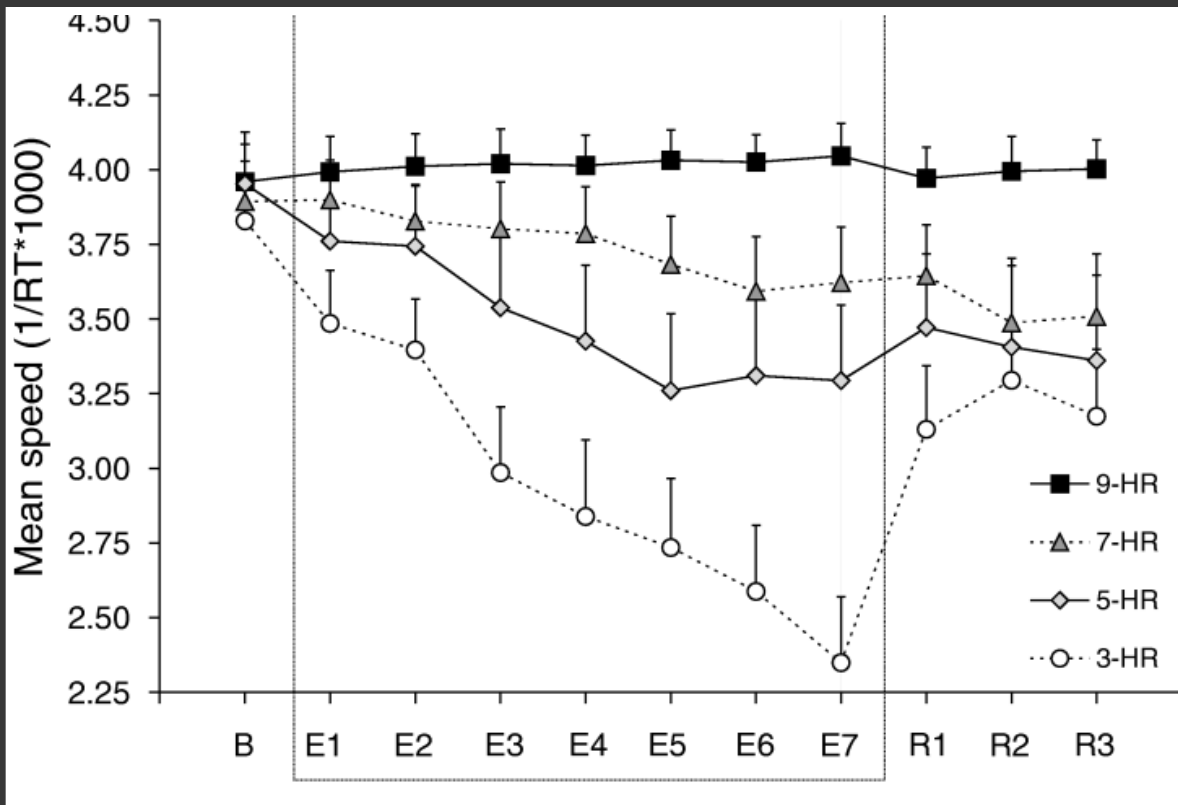
Majority of adolescents do not get adequate sleep.
40% of adults do not get 7-8 hrs sleep.
3% have nodded off driving...in the past month.

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?



Belenky et al., J Sleep Research 2003;12:1-12

STATE OF THE ART (SOTA) IN
HUMANS:
DELAYED/INCOMPLETE
RECOVERY OF ALERTNESS

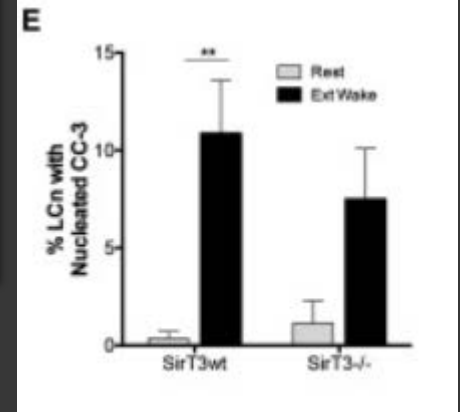
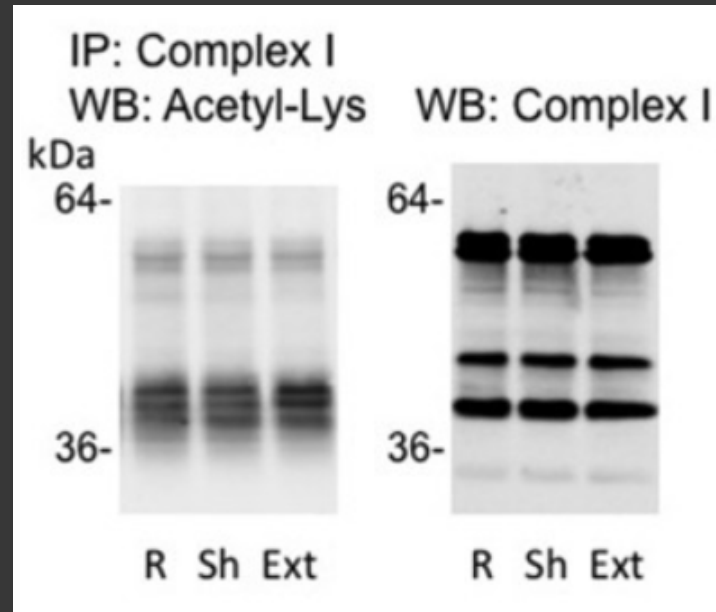
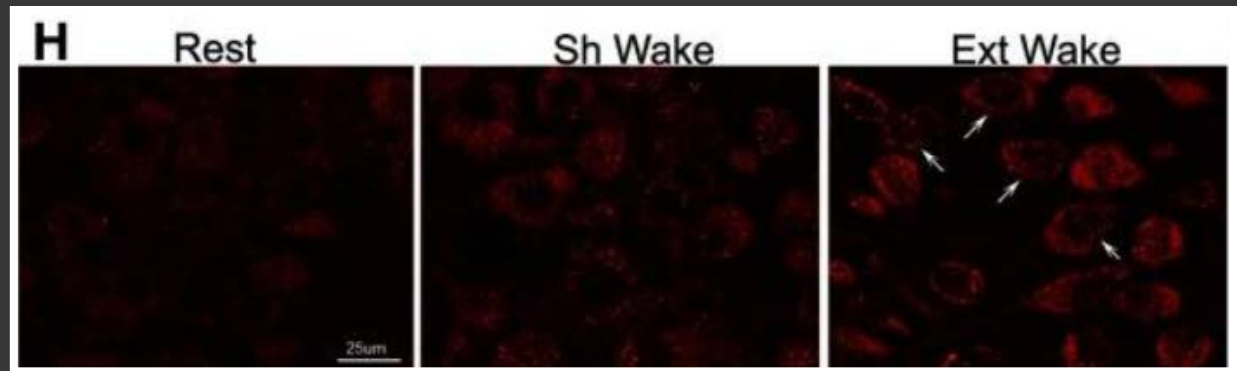
STATE OF THE ART MECHANISMS:

Extended wakefulness:

Locus coeruleus

oxidative stress,

mitochondrial injury & degeneration



CHRONIC INTERMITTENT SLEEP LOSS MODELING SHIFT WORK

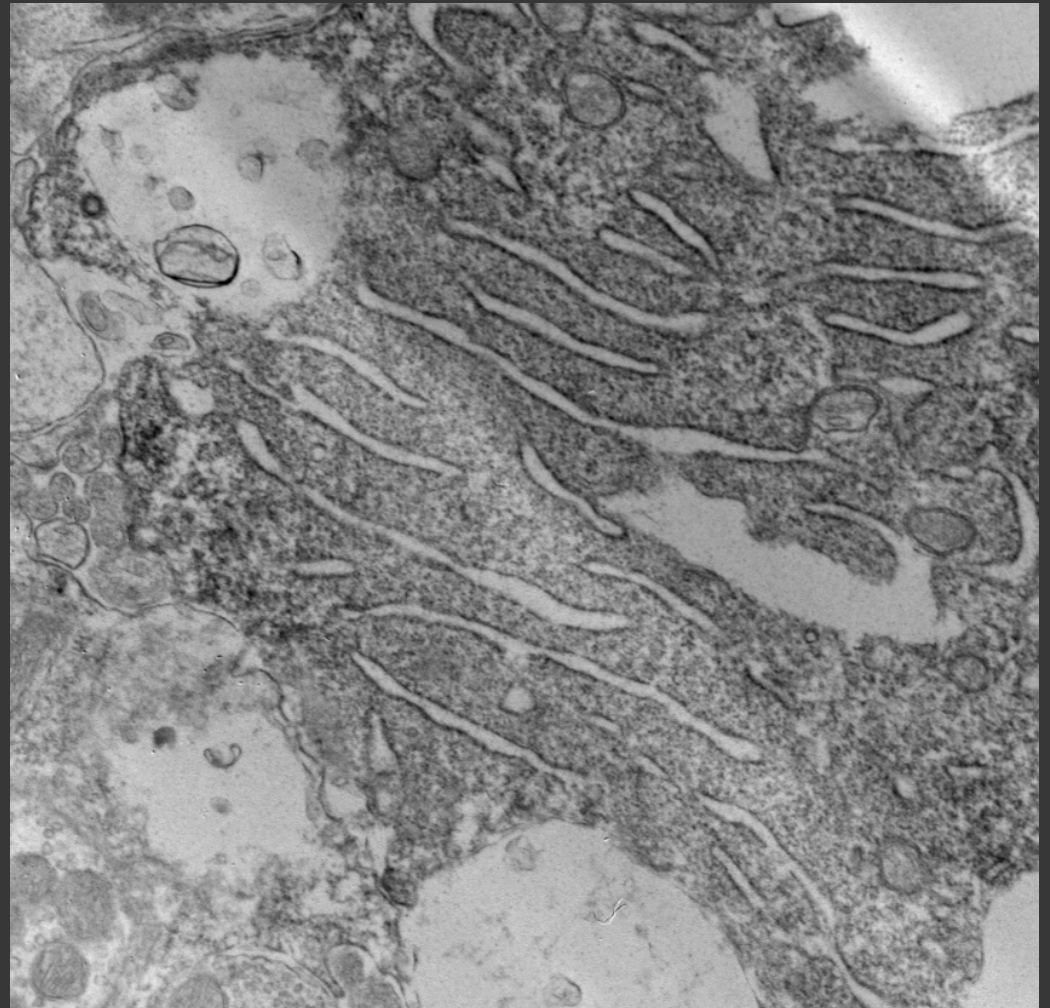
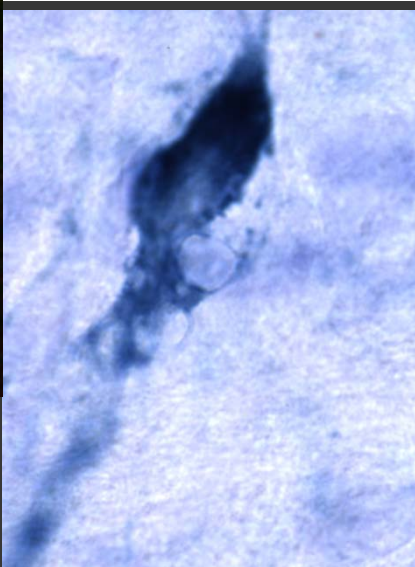
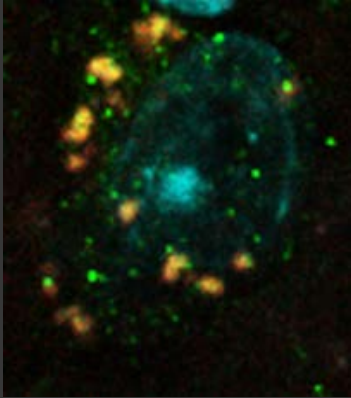
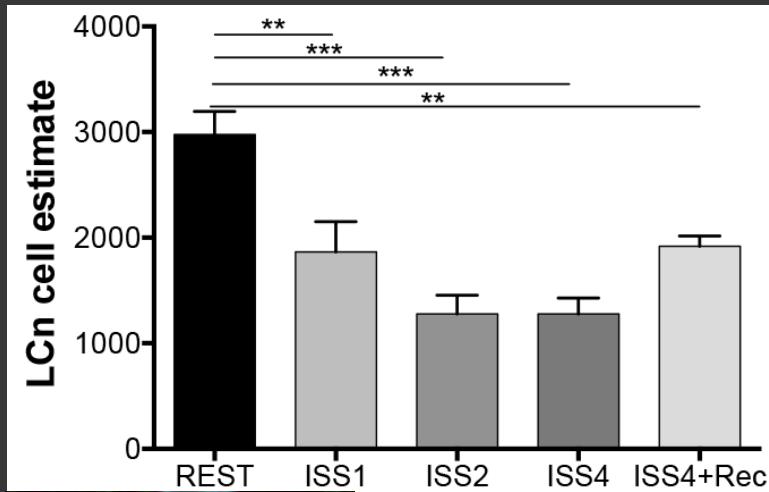


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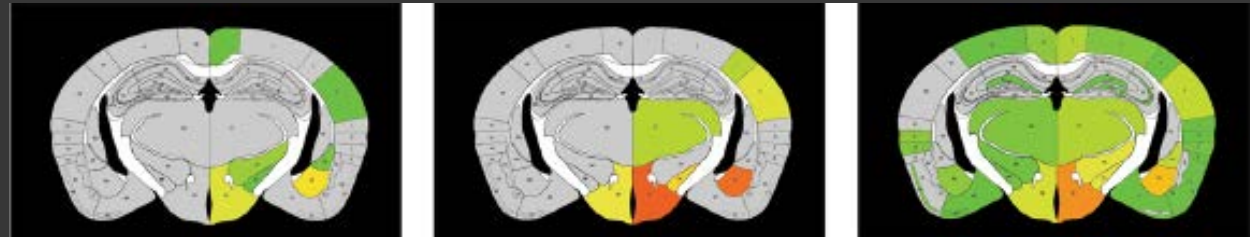
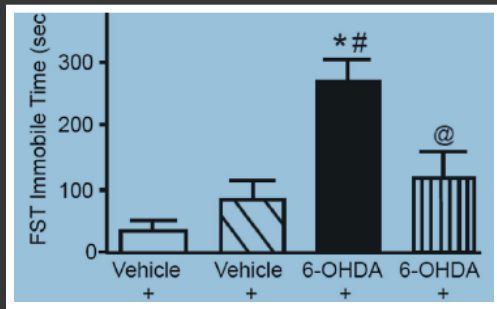
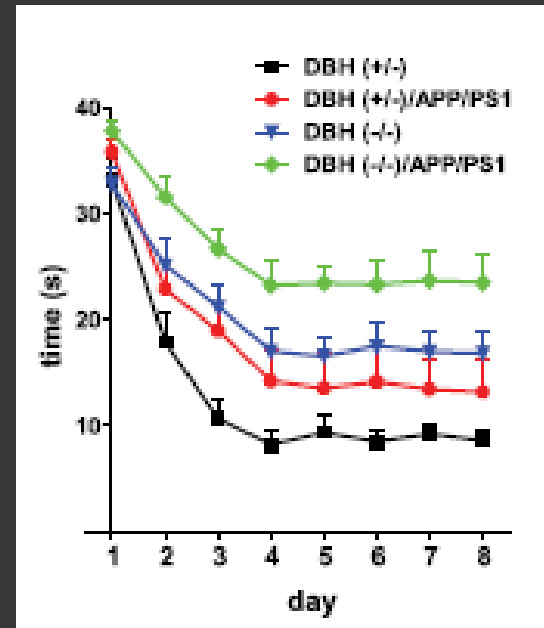
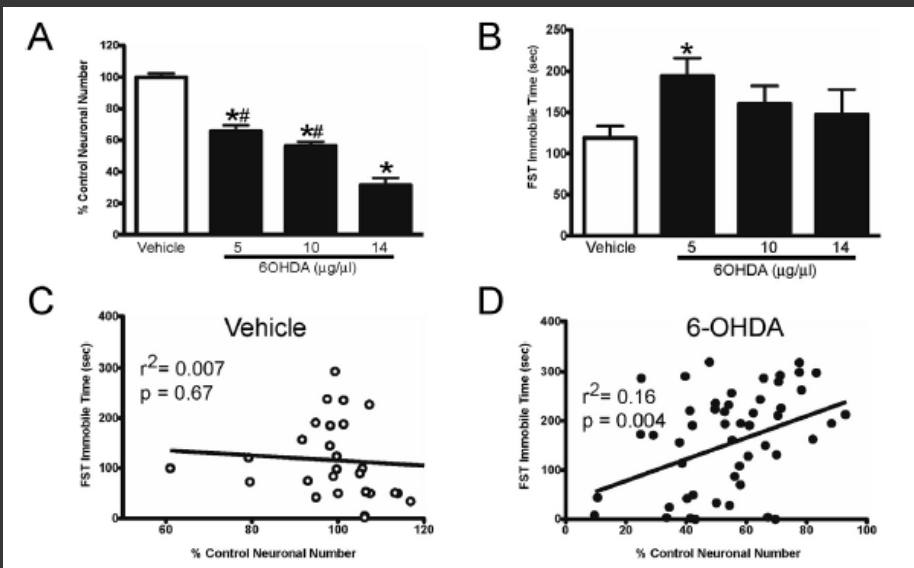
Chronic short sleep 4 hr less/24hr period

STATE OF THE ART RECOVERY LOSS OF LOCUS COERULEUS NEURONS



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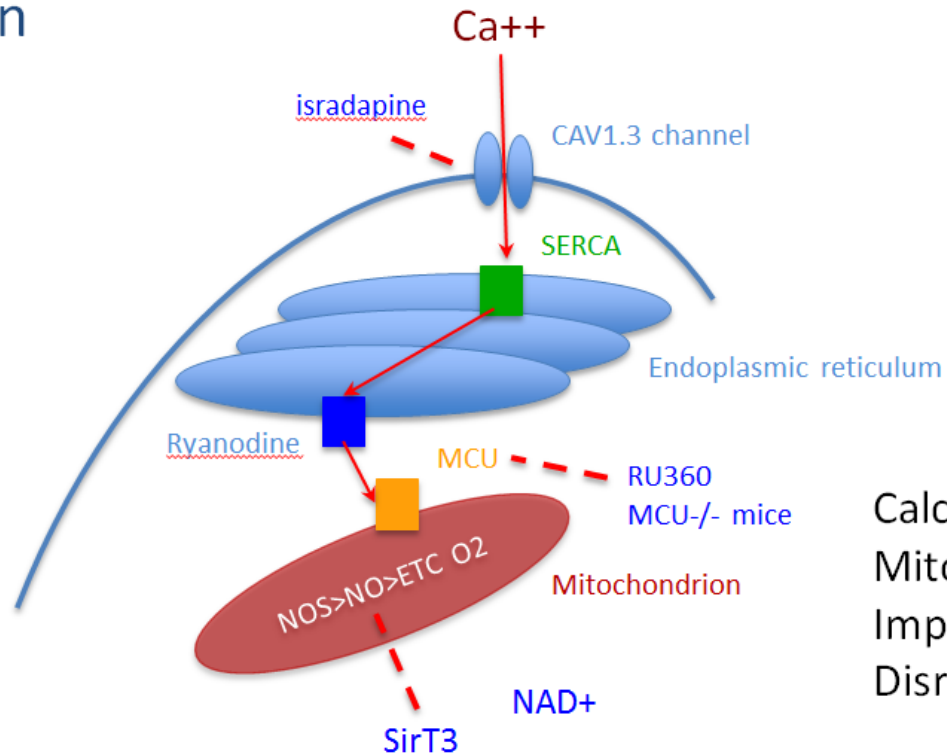
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LC LOSS: DEPRESSION AND ALZHEIMER'S PROGRESSION

KNOWLEDGE GAPS: THE SWITCH

Locus coeruleus
neuron



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?

VEASEY LAB SUMMMER 2015



NIH HLBI R01 079588; R01 124576; R01 123331