

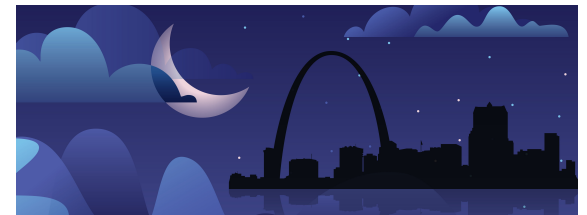


MY BEESON JOURNEY

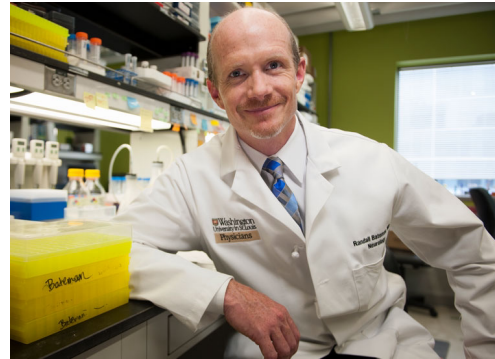
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My Beeson Journey Begins...



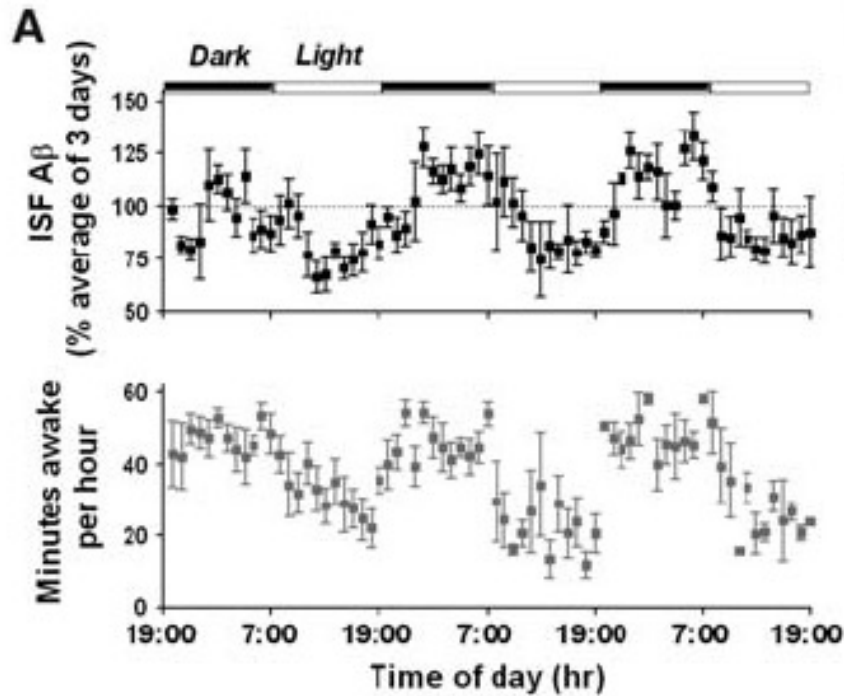
Grandpa
David Holtzman
Beeson 1995

Papa
Randall Bateman
Beeson 2007

Me
Beeson 2016

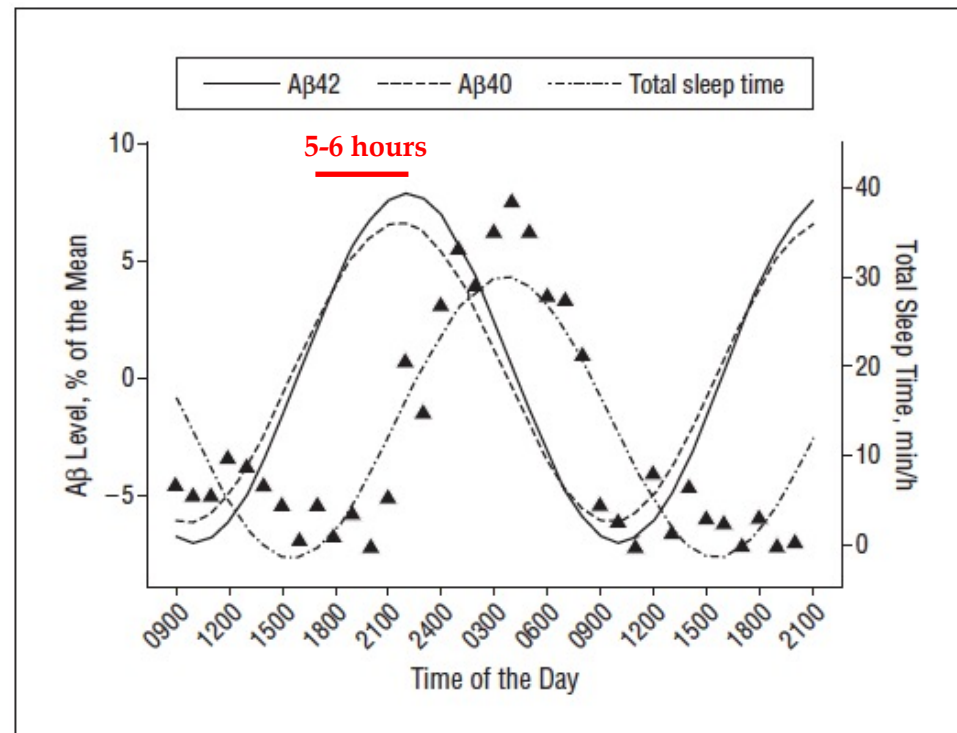
A β Fluctuates with Sleep-Wake Activity

Mice



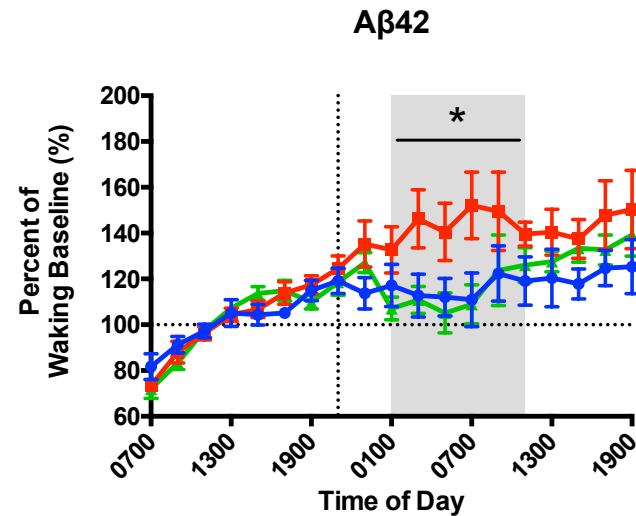
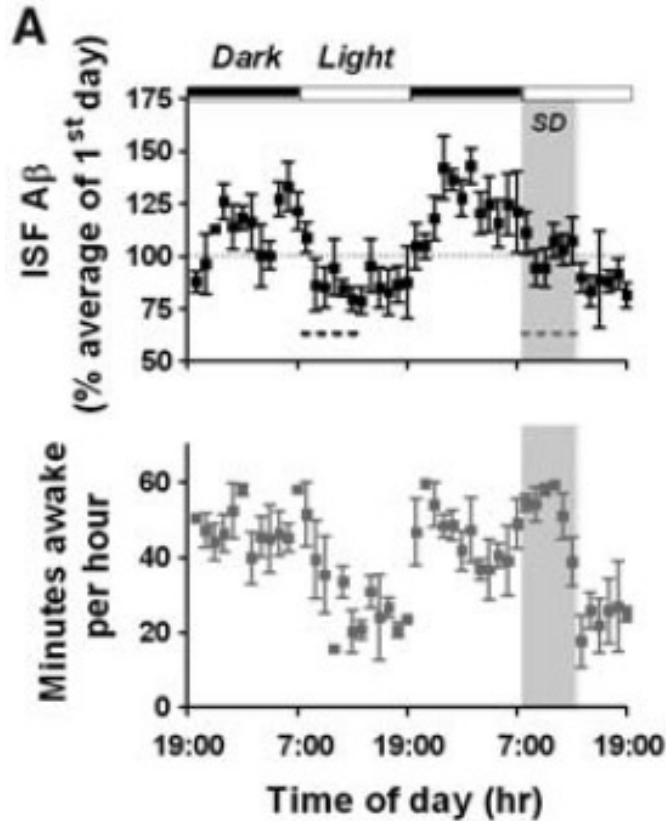
Kang JE, et al., Science 2009; 326:1005

Humans



Huang Y, et al., Arch Neurol 2012; 69:51

Sleep Deprivation and ISF/CSF A β

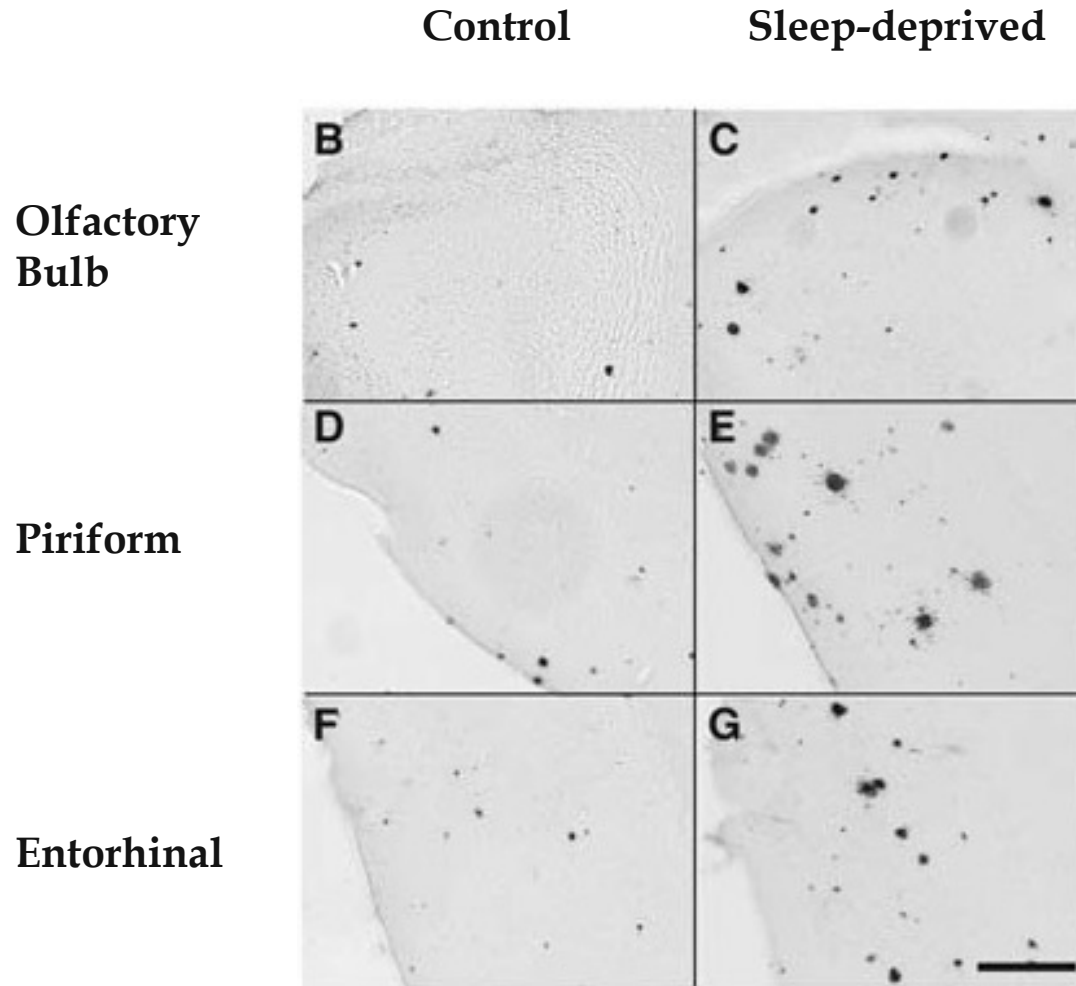


Blue=Control; Red=Sleep-deprived; Green=Drug

Lucey BP, et al., Ann Neurol 2018; 83:197

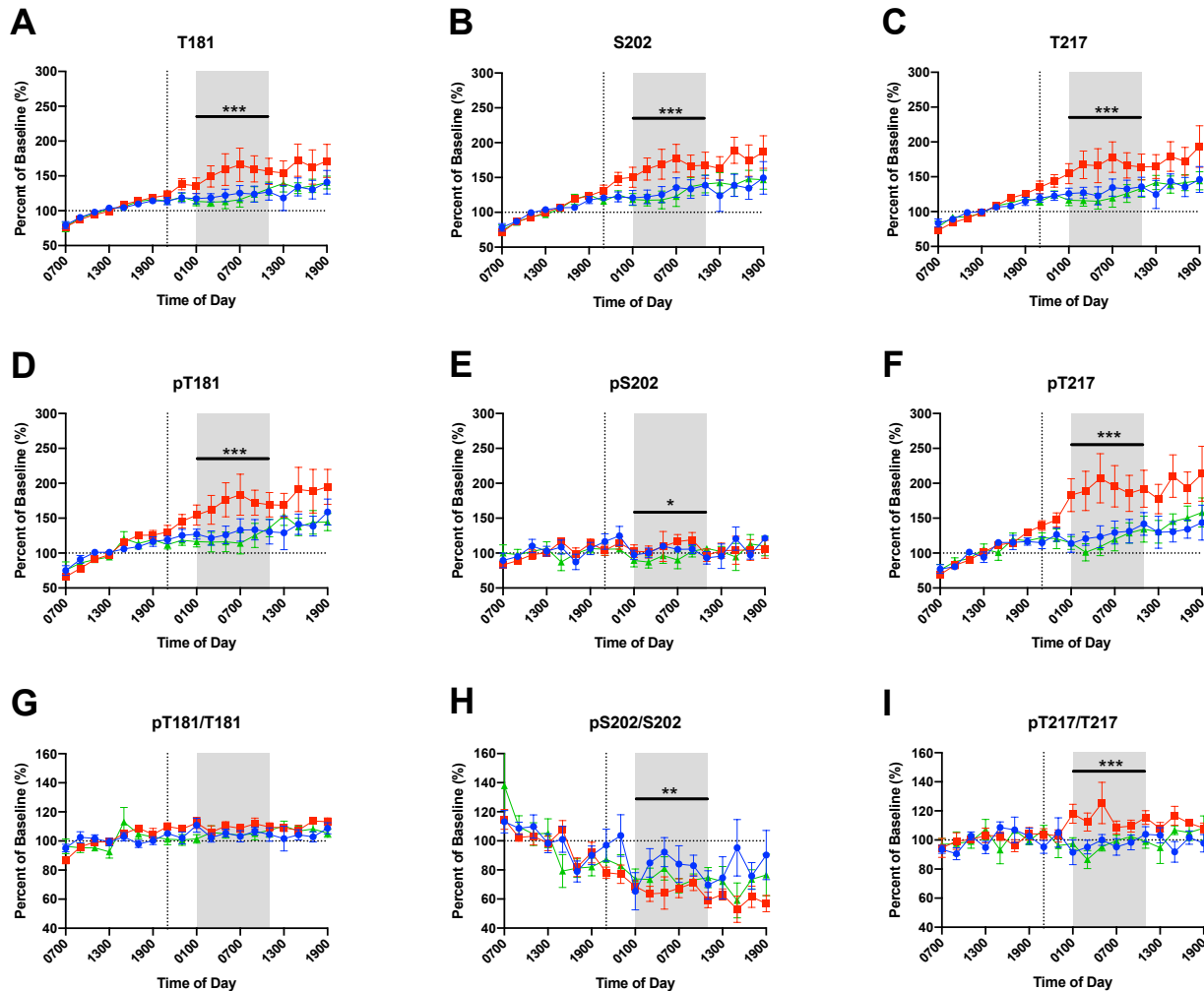
Kang JE, et al., Science 2009; 326:1005

Sleep Deprivation Affects A β Pathology



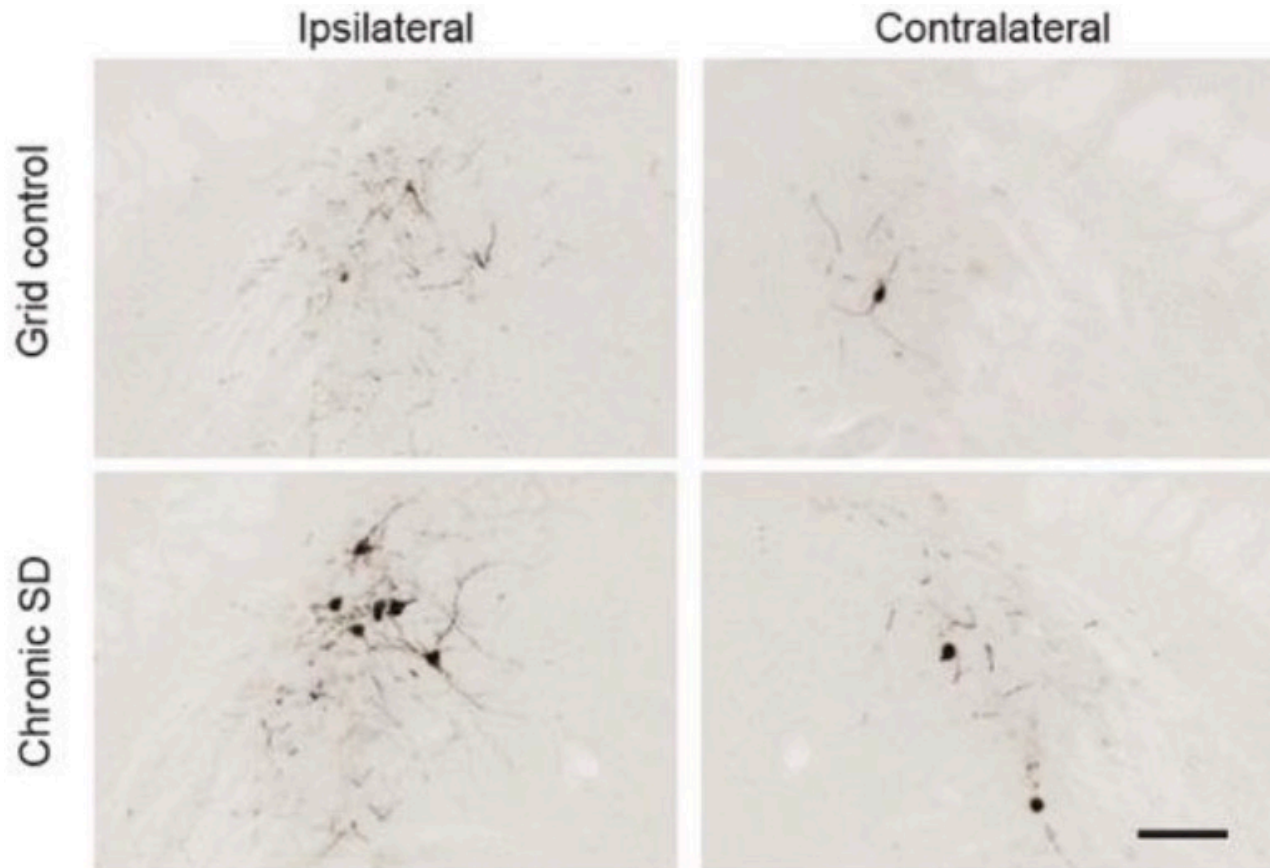
Kang JE, et al., Science 2009; 326:1005

Sleep Deprivation Increases CSF Tau, But Tau Phosphorylation Is Site Specific



Barthelemy NR, et al.,
Ann Neurol 2020;
87:700

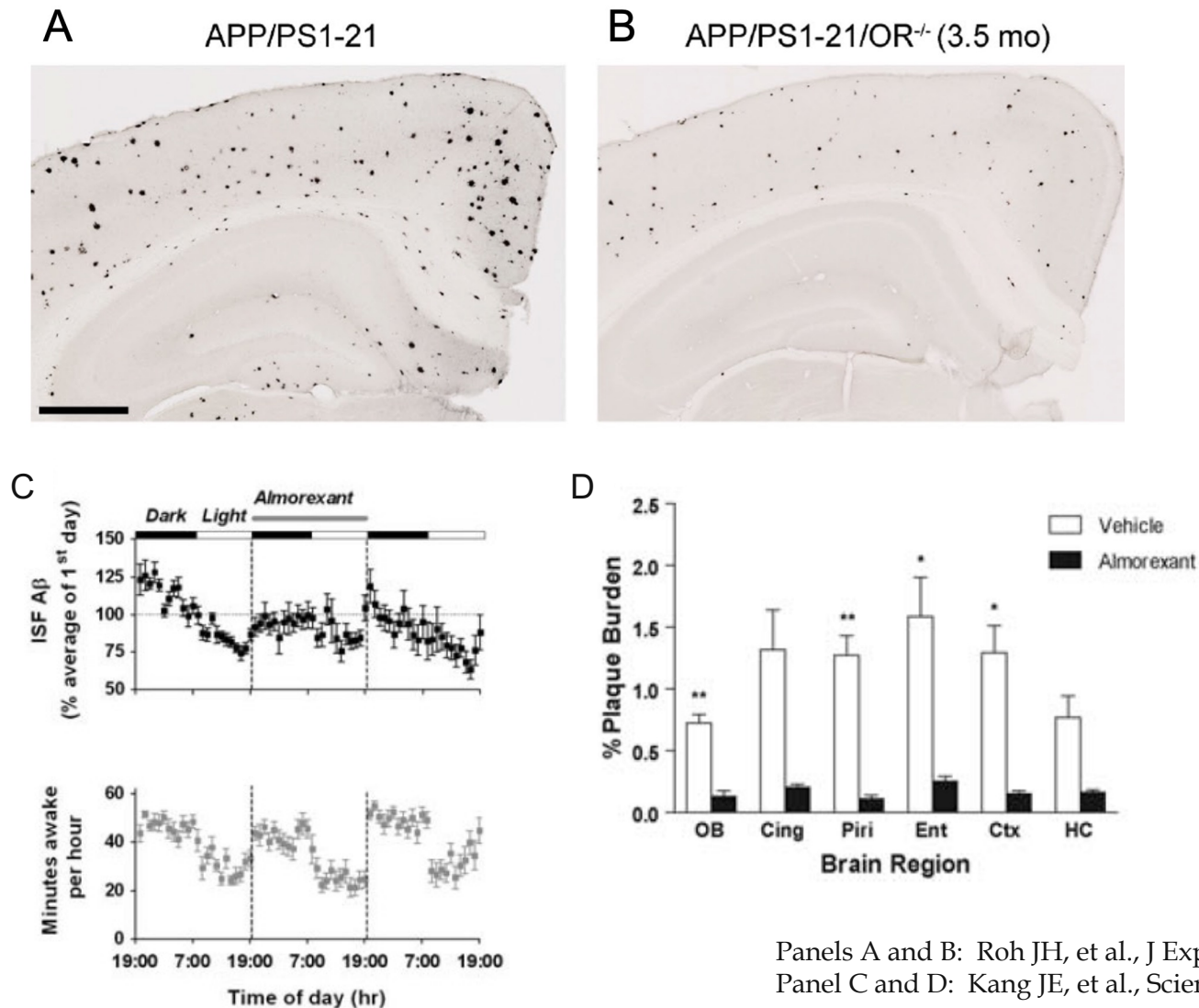
Sleep Deprivation Increases Tauopathy



Locus ceruleus

Holth JK, et al., Science 2019; 363:880

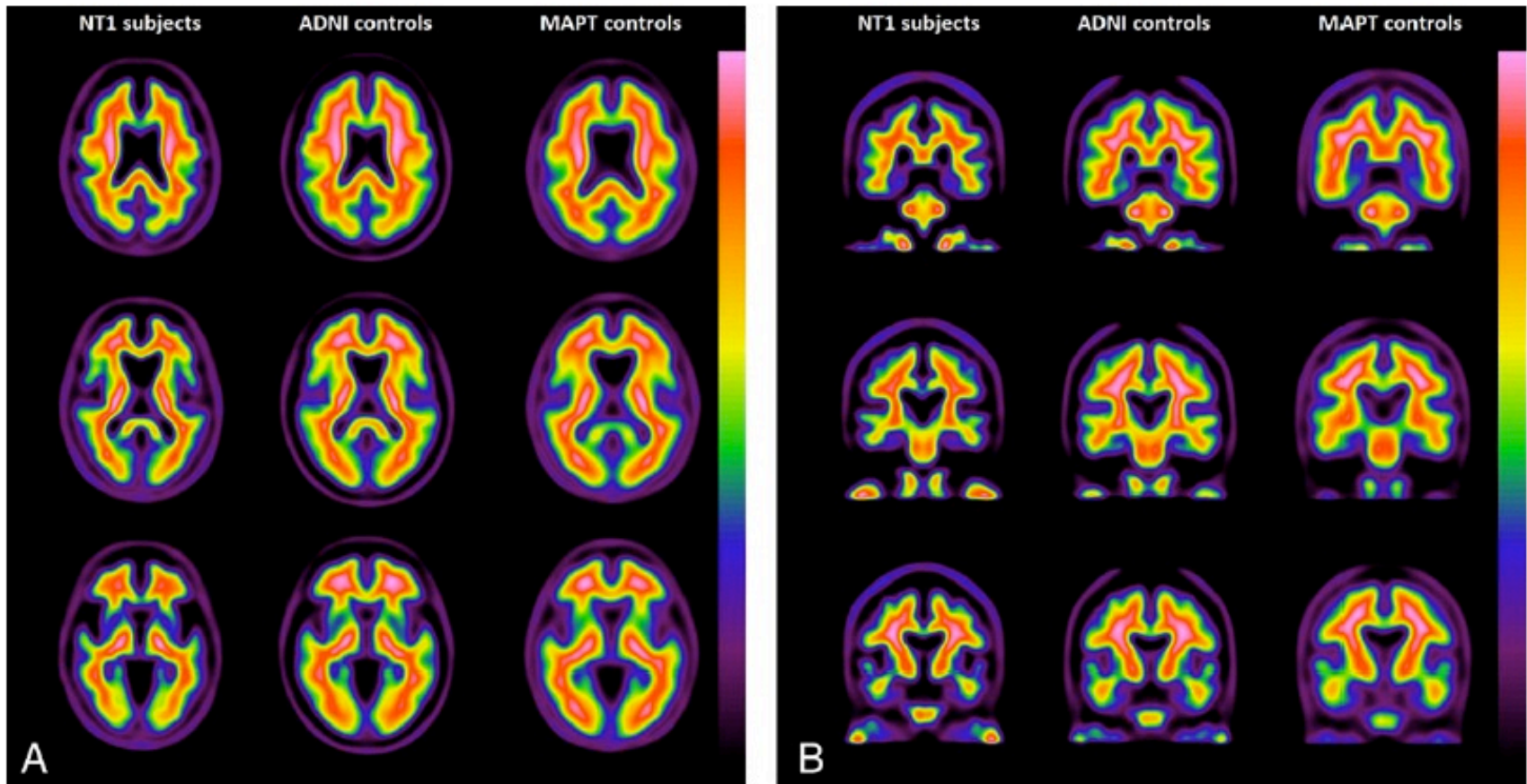
Orexin and AD Pathology



Panels A and B: Roh JH, et al., J Exp Med. 2014; 211: 2487

Panel C and D: Kang JE, et al., Science. 2009; 326: 1005

Orexin and AD Pathology

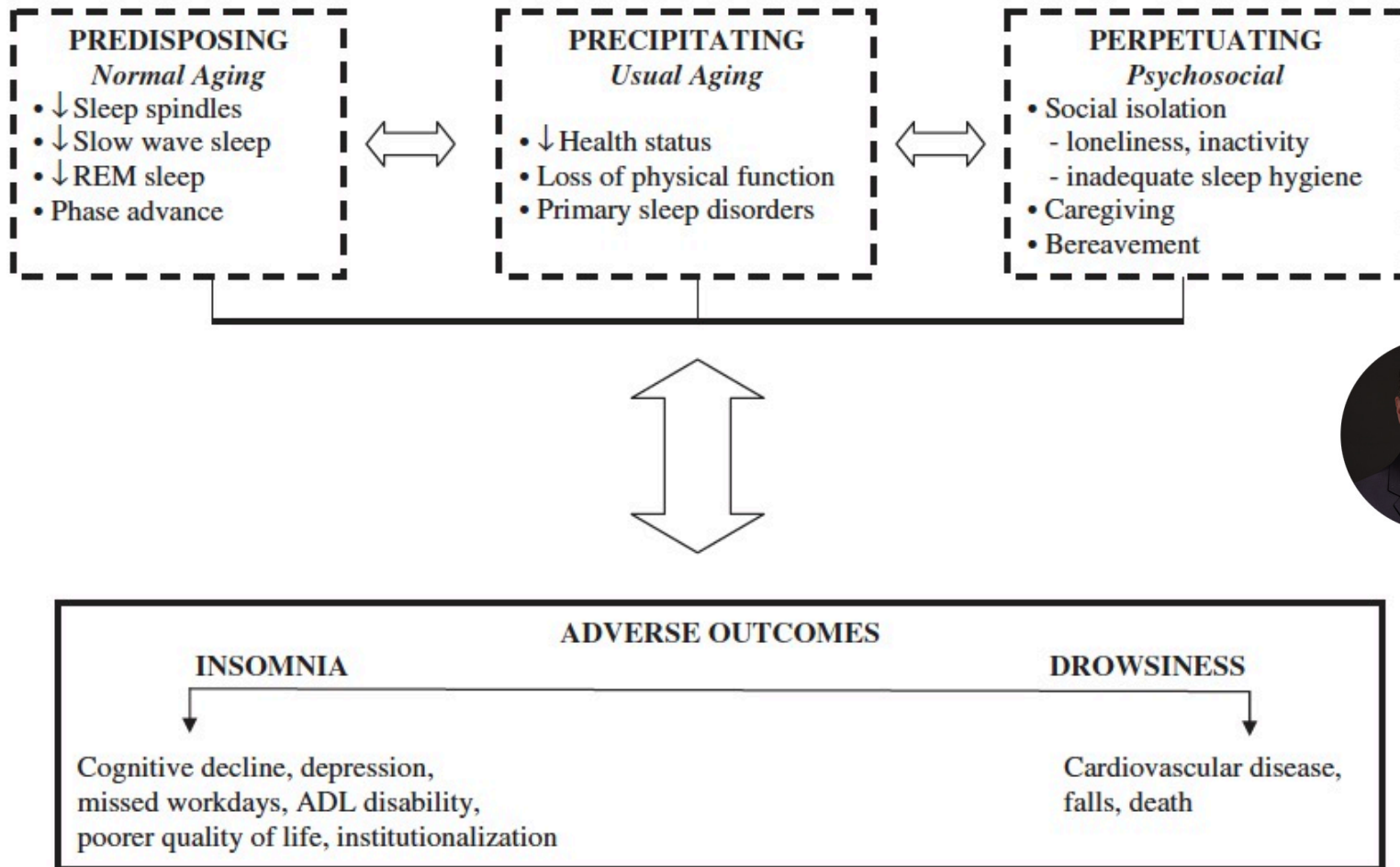


Gabelle A, et al., Ann Neurol 2019; 85:74

Beeson Goals

- Project aims:
 1. To determine if CSF A β levels are lower in cognitively normal individuals 45-65 years old with poor vs. good sleep efficiency (time asleep/time in bed)
 2. To determine if CSF A β levels are lower in cognitively normal individuals 45-65 years old with poor sleep efficiency treated with suvorexant (a dual orexin receptor antagonist FDA-approved to treat insomnia) vs. placebo

Sleep Disturbances in Older Adults: A Multifactorial Geriatric Syndrome



Vaz Fragoso CA, Gill TM, J Am Geriatr Soc 2007; 55:1853

Future Directions

- Preliminary data from the Beeson directly lead to \$9.4 million in funding from Open Philanthropy / Good Ventures to support a trial testing the effect of suvorexant on amyloid PET in cognitively normal amyloid-positive adults 65 years and older
- Industry-sponsored study
- A major future goal is to test the effect of different doses of suvorexant and other drugs in the same class on CSF AD biomarkers
 - Suvorexant (approved 2015)
 - Lemborexant (approved 2020)
 - Others in the pipeline

Thank You!

- Randall Bateman
- David Holtzman
- Participants
- Beeson Community

Family

Lucey Lab

Cristina Toedebusch
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Rachel Richardson
Scott Sauers
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William Lu

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Vitaliy Ovod
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John Morris
Bruce Patterson
Donald Elbert