MY BEESON JOURNEY

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My Beeson Journey Begins…

Grandpa
David Holtzman
Beeson 1995

Papa
Randall Bateman
Beeson 2007

Me
Beeson 2016
Aβ Fluctuates with Sleep-Wake Activity

Mice


Humans

Huang Y, et al., Arch Neurol 2012; 69:51
Sleep Deprivation and ISF/CSF Aβ


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

Blue=Control; Red=Sleep-deprived; Green=Drug
Sleep Deprivation Affects Aβ Pathology

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

Orexin and AD Pathology


Orexin and AD Pathology

Beeson Goals

- **Project aims:**
  1. To determine if CSF Aβ 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 Aβ 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

PREDISPOSING
Normal Aging
- ↓ Sleep spindles
- ↓ Slow wave sleep
- ↓ REM sleep
- Phase advance

PRECIPITATING
Usual Aging
- ↓ Health status
- Loss of physical function
- Primary sleep disorders

PERPETUATING
Psychosocial
- Social isolation
- Loneliness, inactivity
- Inadequate sleep hygiene
- Caregiving
- Bereavement

ADVERSE OUTCOMES

INSOMNIA
- Cognitive decline, depression,
  missed workdays, ADL disability,
  poorer quality of life, institutionalization

DROWSINESS
- Cardiovascular disease,
  falls, death

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

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Family