

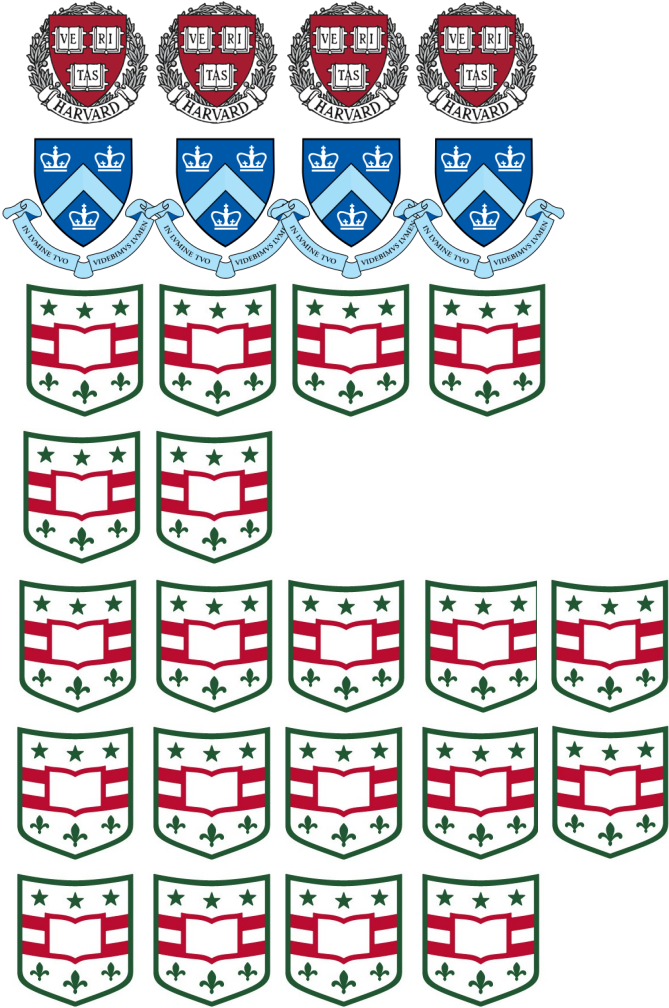
Sleep & Neurodegeneration

WashU Parents' Council

Yo-El Ju, MD MSCI

2 November 2024

Background



Group (L -> R)

Flavia Fagundes Bueno
Jennifer McLeland
Leah Taylor
Maggie Zangrilli
Jill Boyd
Ellen Fischbach
Raiyan Hamilton

(Indiv, top down)

Jason Dude
Kristina Hedtkamp
Sunita Loum
Peter Tran

Not pictured

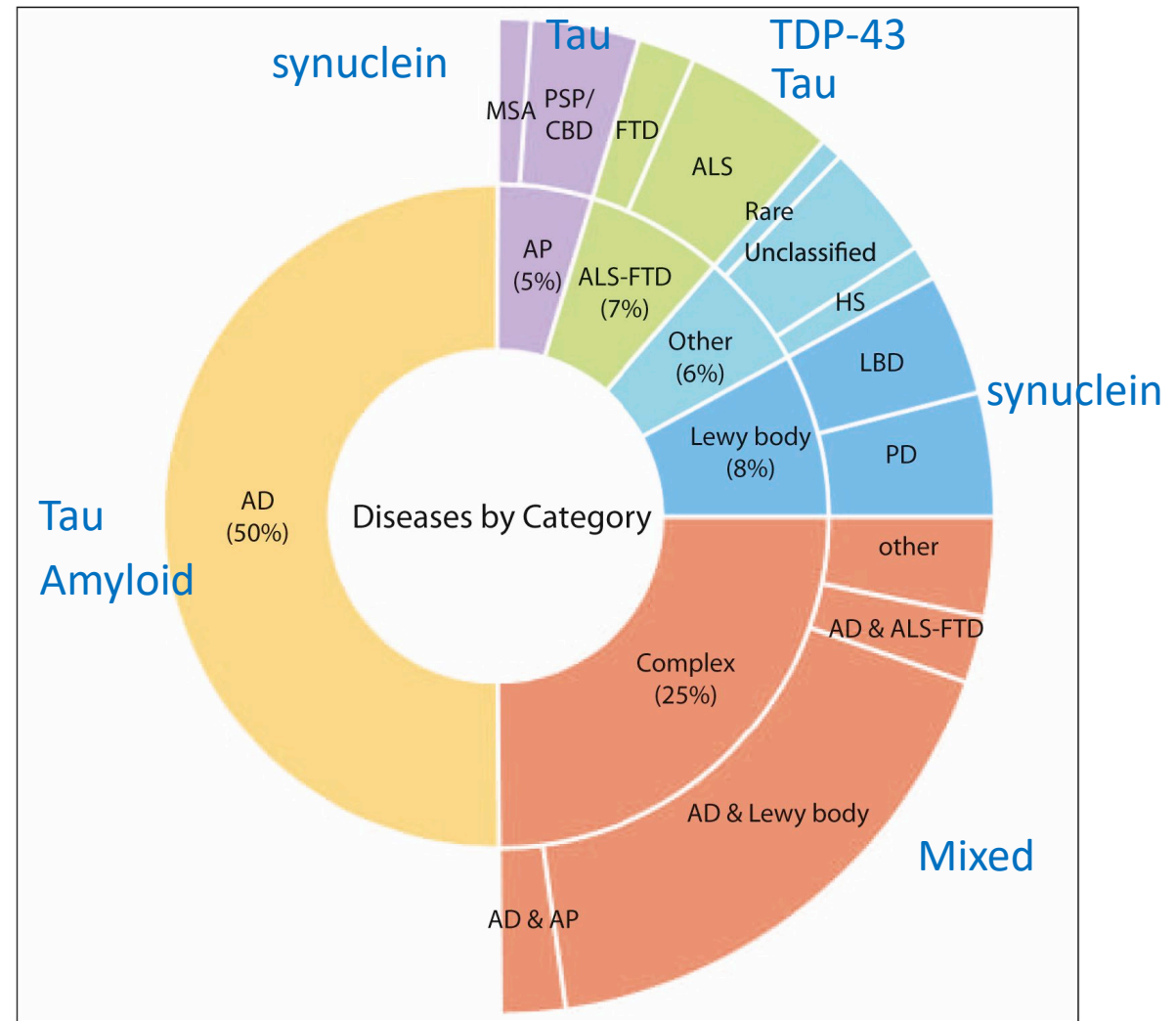
Annabelle Yang
Katie Madden
Nithya Chennupati

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Neurodegenerative Diseases

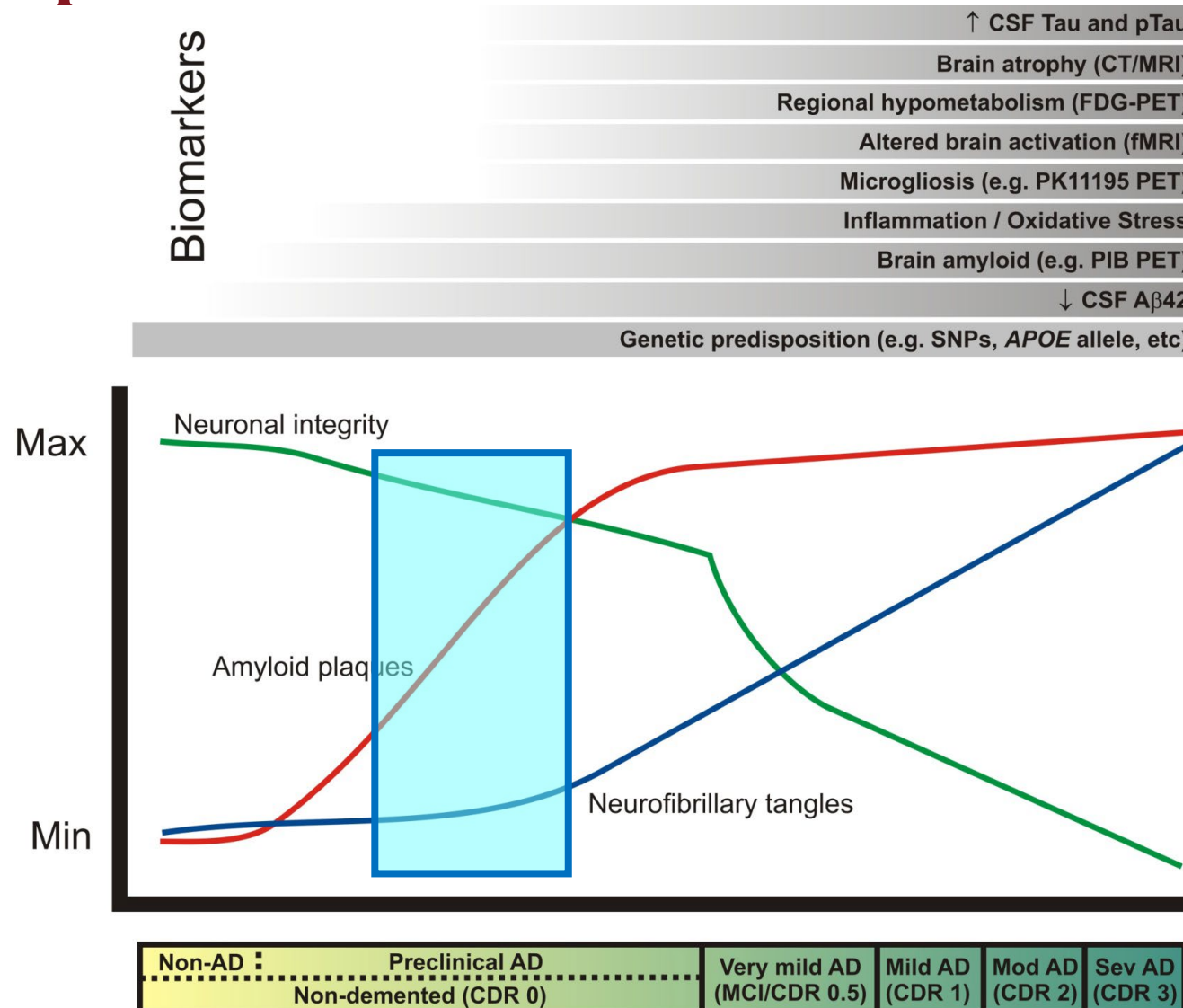
- Death of previously-healthy, specific neuronal populations
- Risk increases with age
- ~7M Americans, \$500B/yr
- Protein aggregation is a common underlying mechanism – and method of categorization



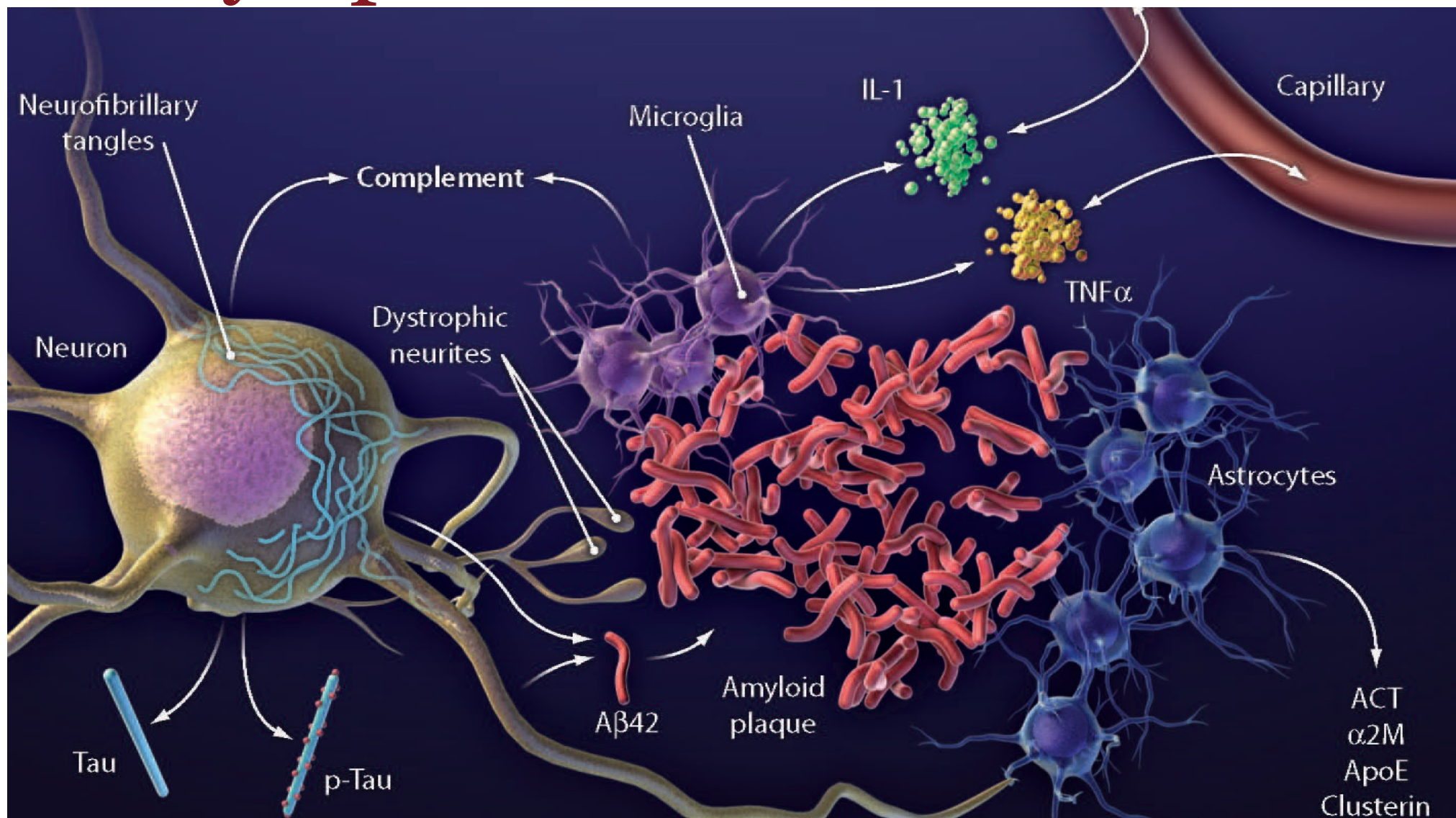
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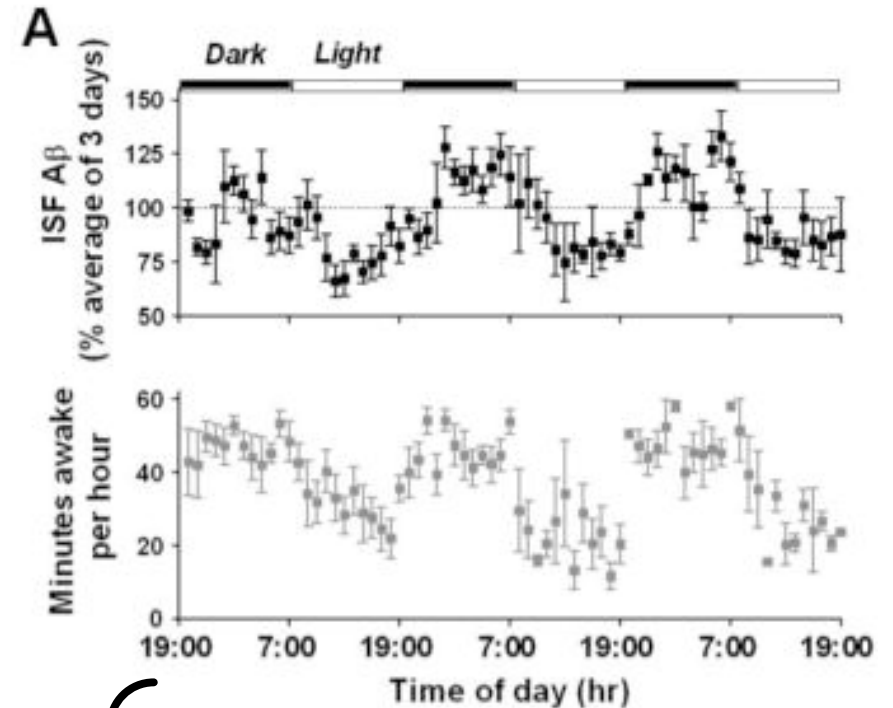
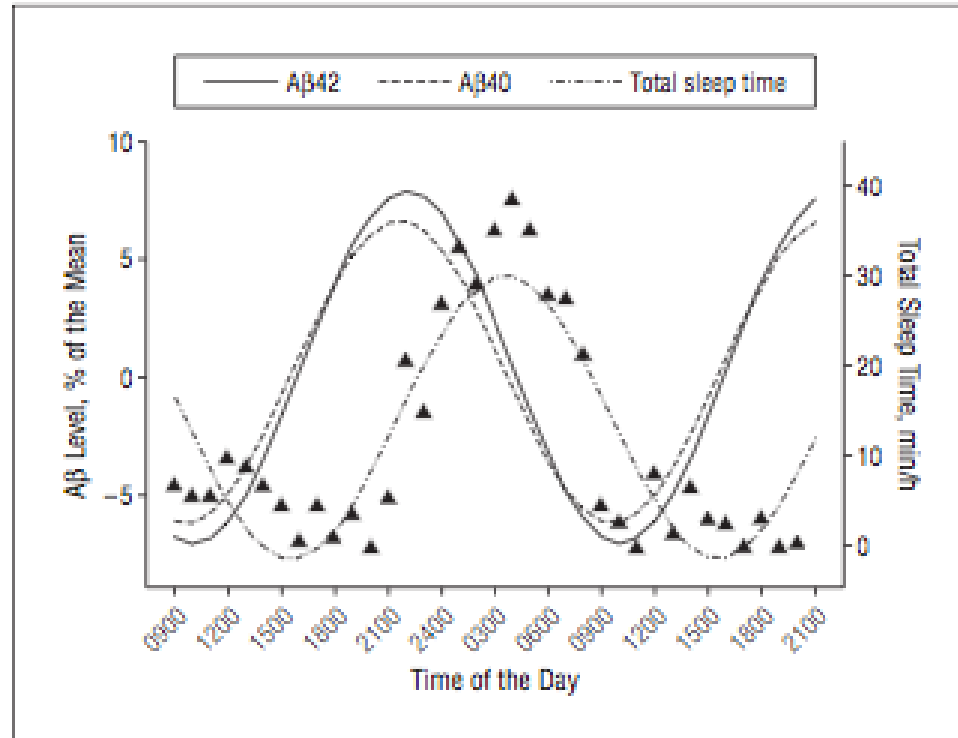
Neurodegenerative Diseases begin years before symptoms



Neurodegenerative Diseases begin years before symptoms



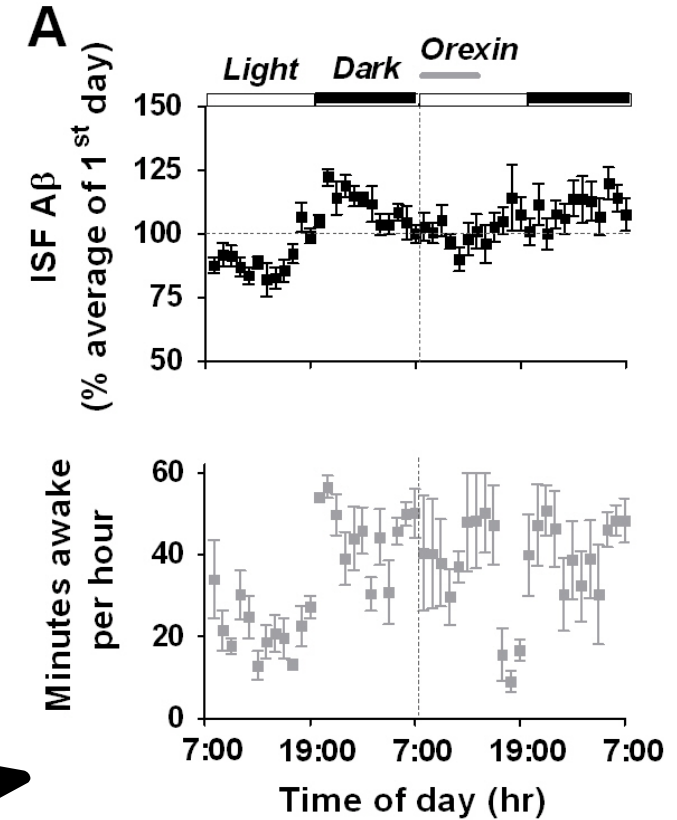
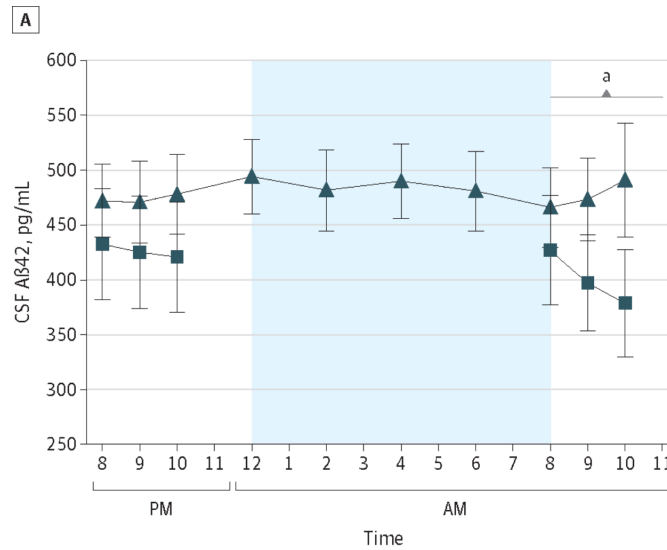
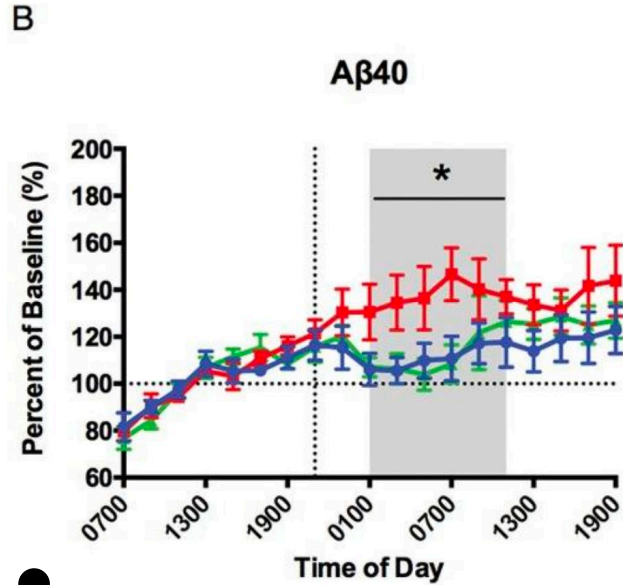
A β decreases during sleep and increases during wake



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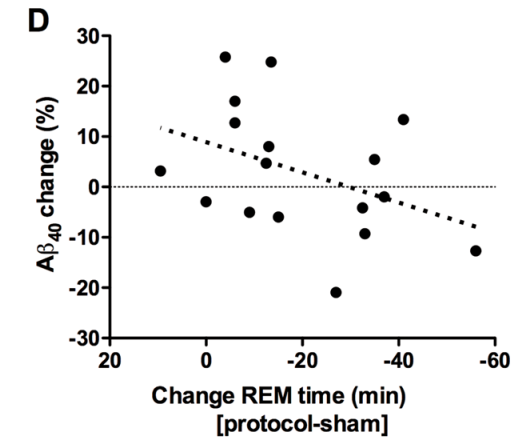
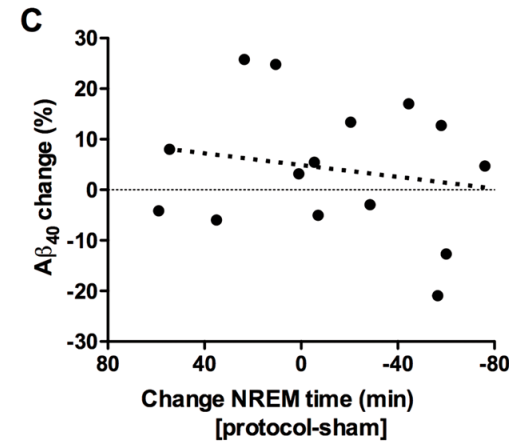
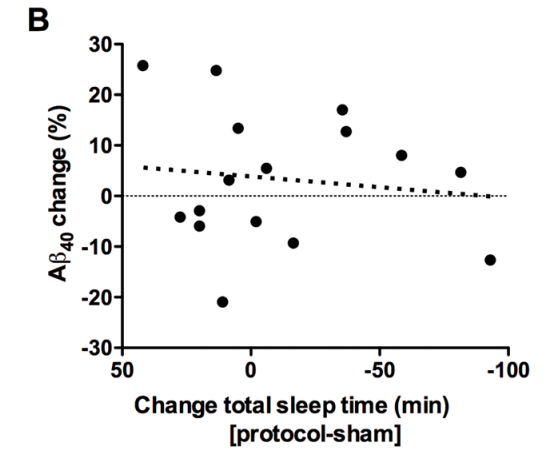
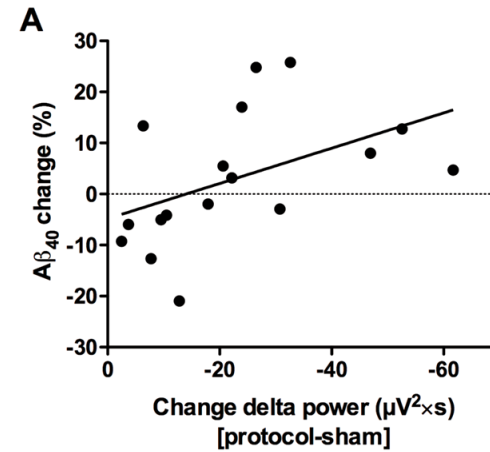
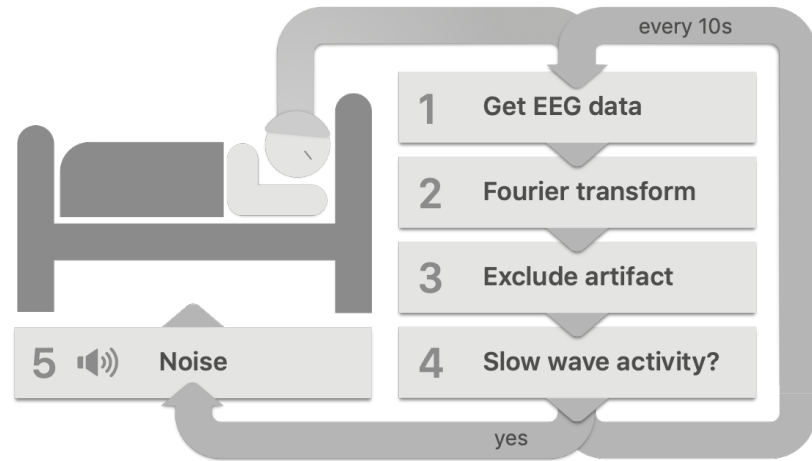
Sleep deprivation increases A β



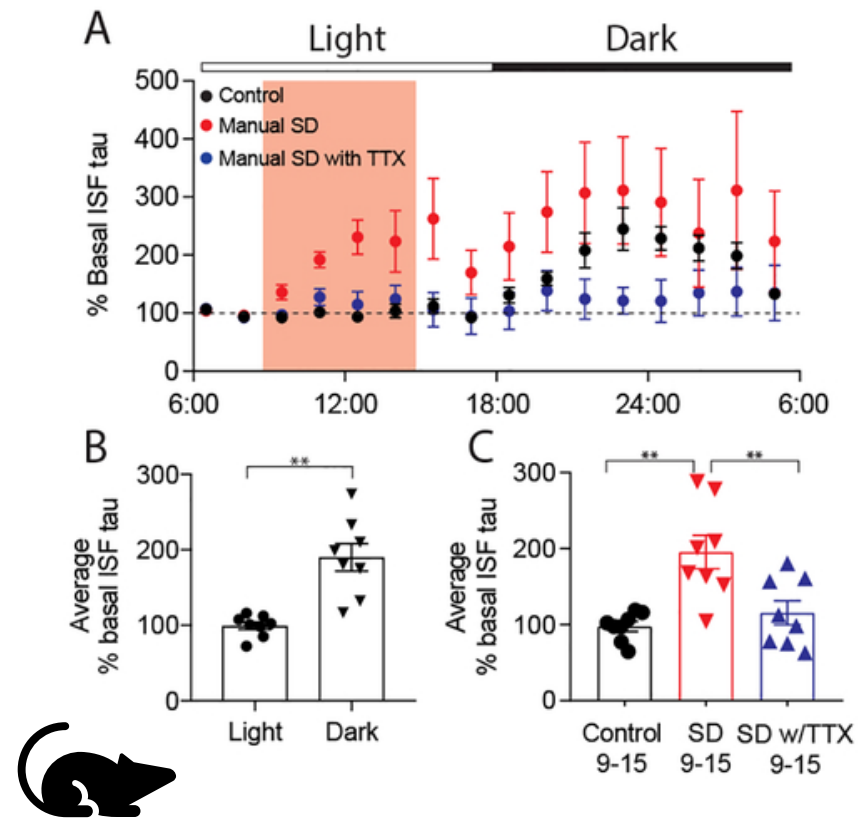
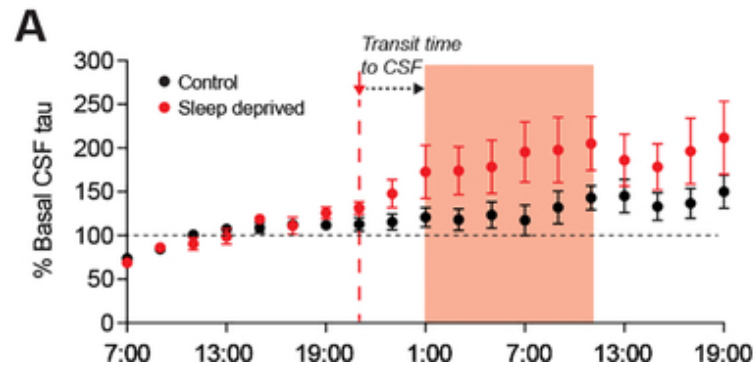
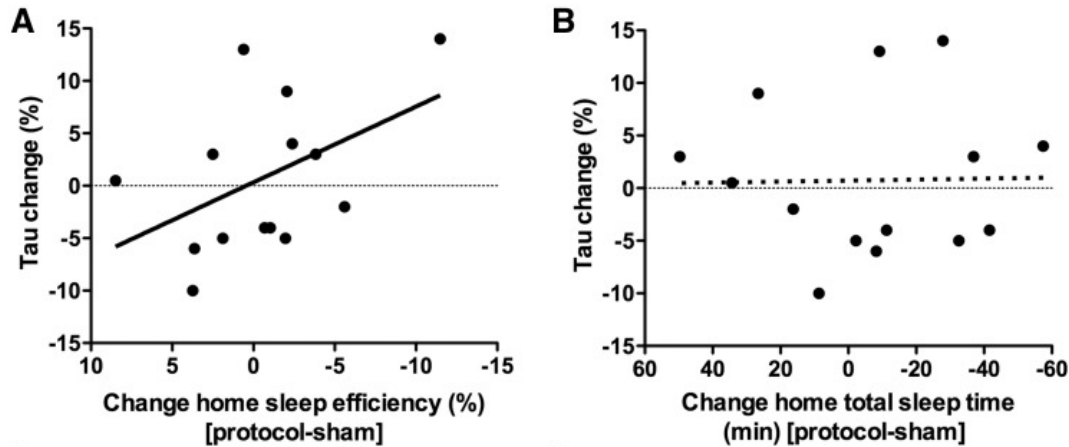
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Slow wave sleep disruption increases $A\beta$



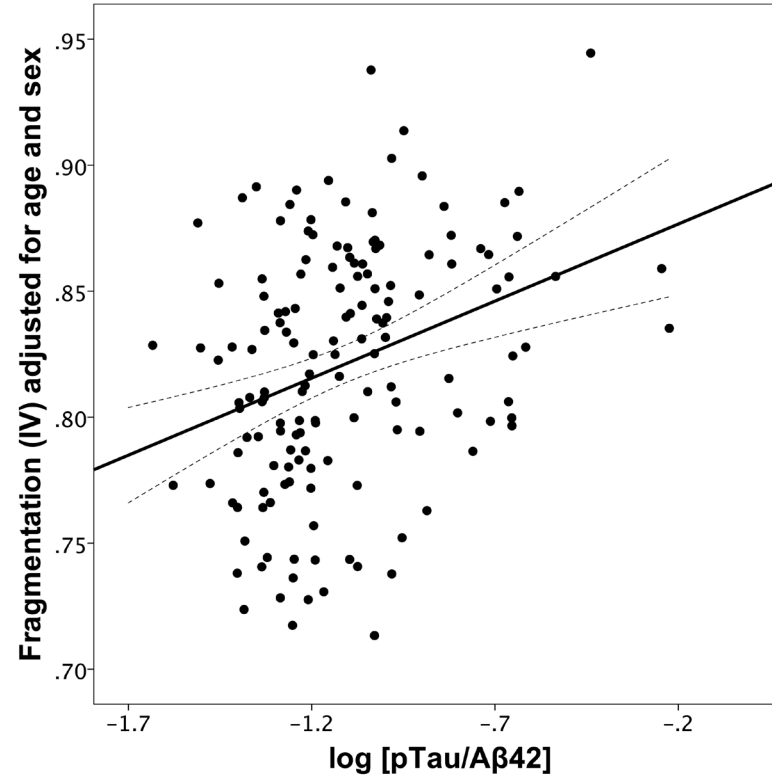
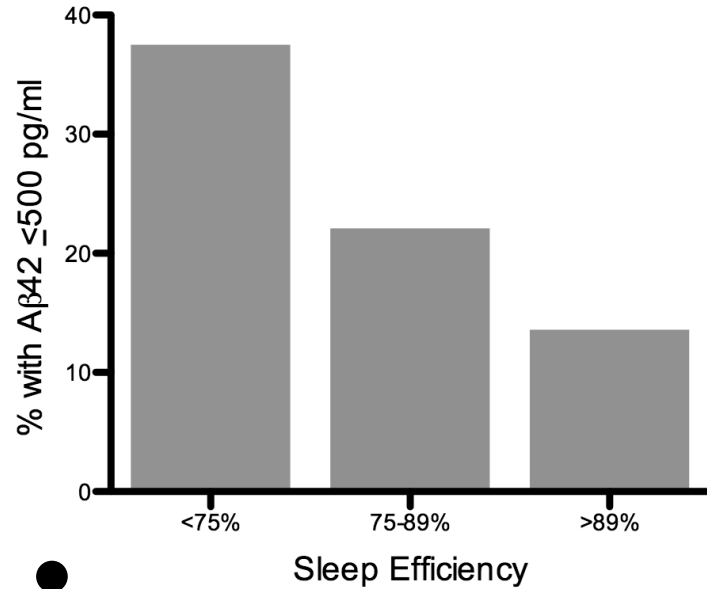
Sleep disruption increases Tau



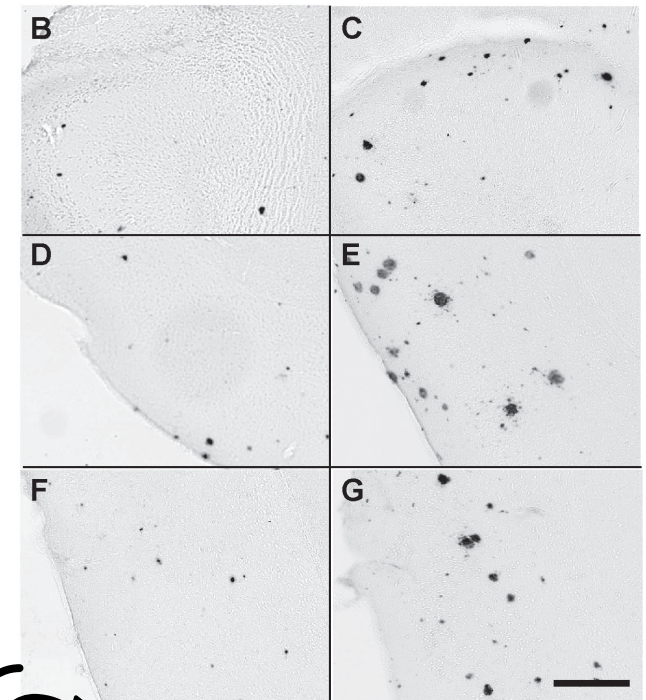
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Sleep disruption is associated with amyloid plaques

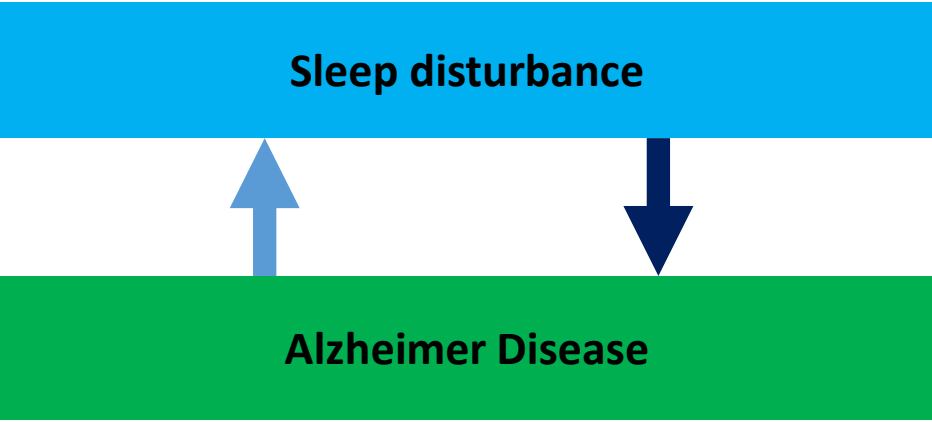


Control Sleep deprivation



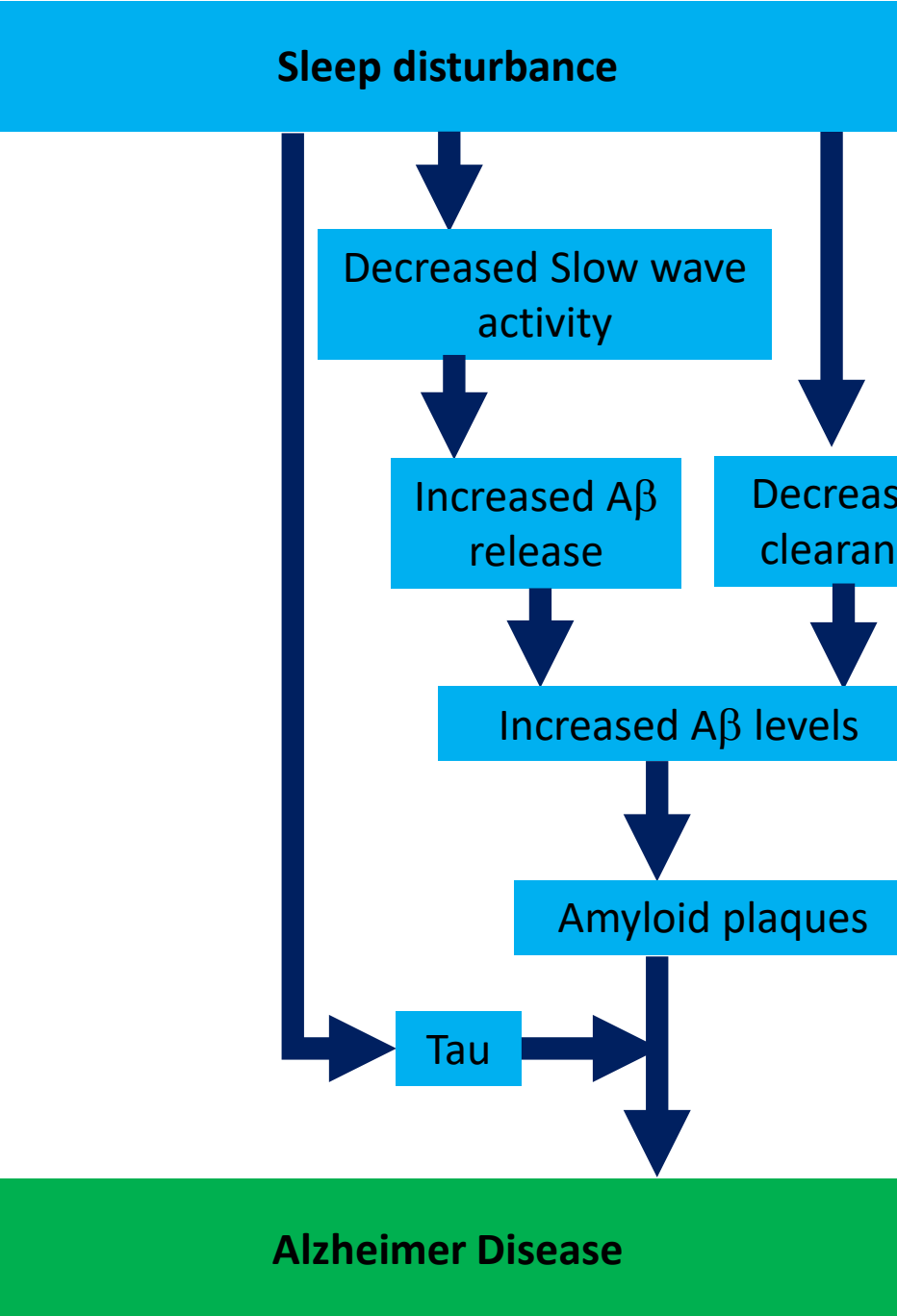
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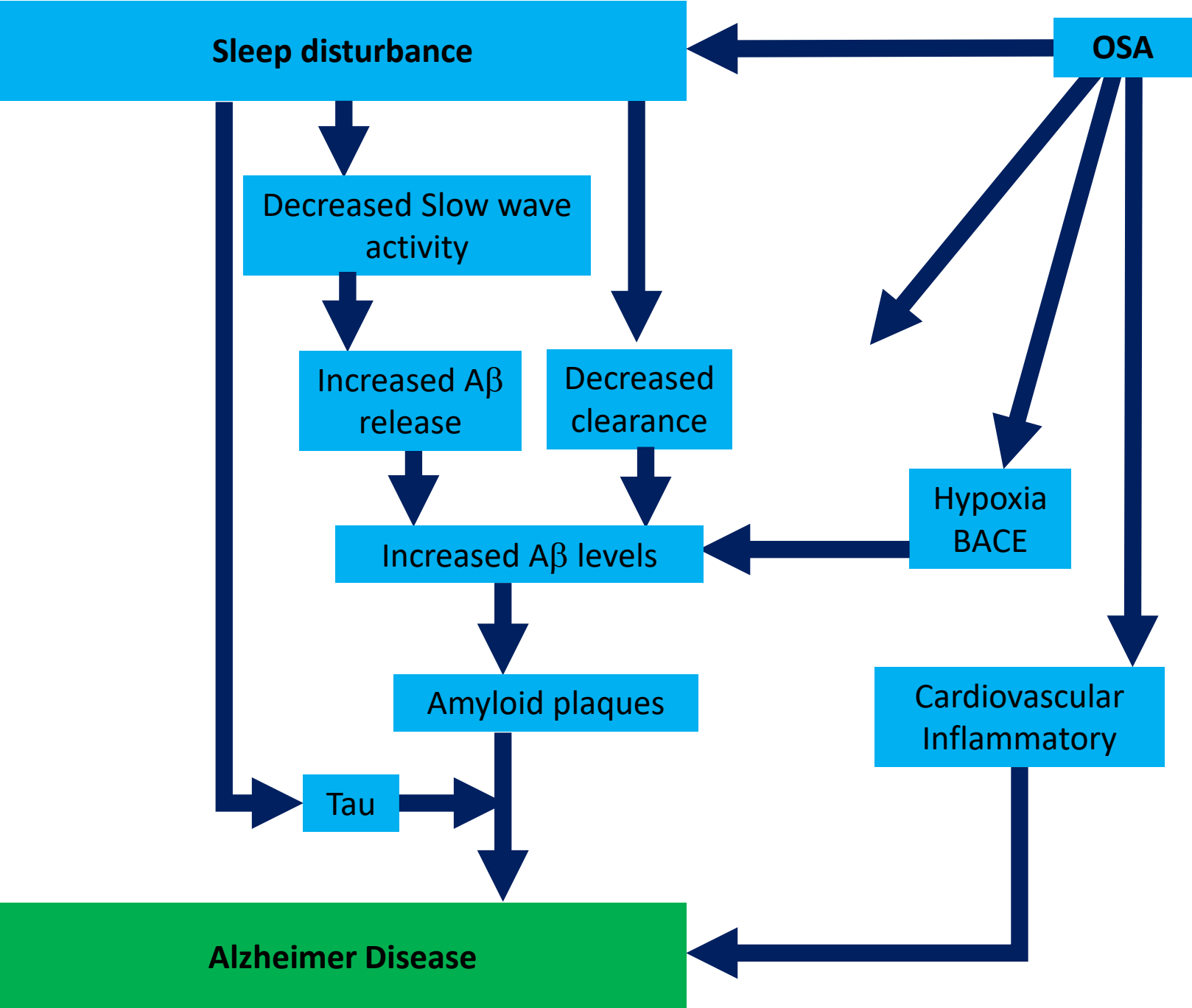
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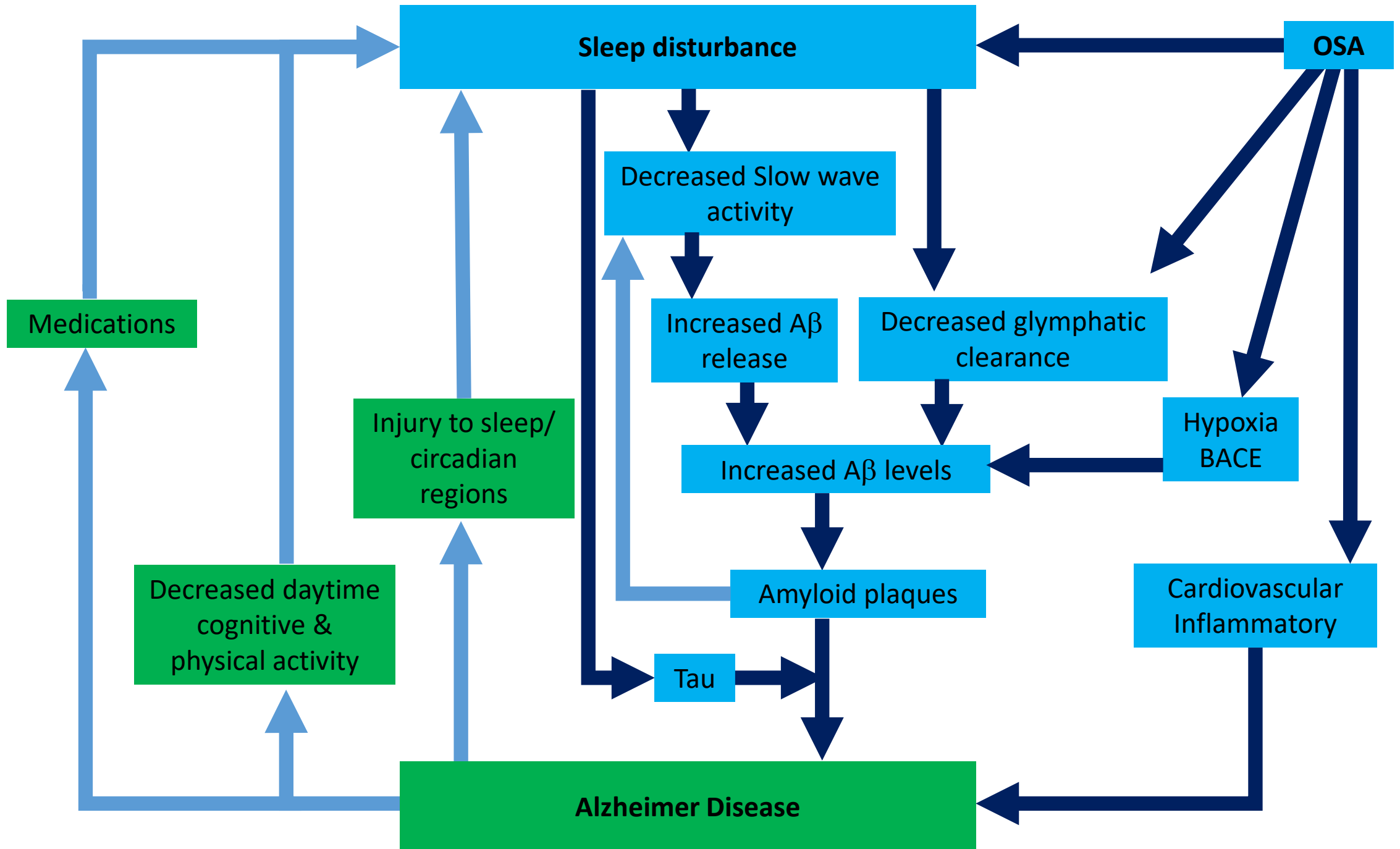


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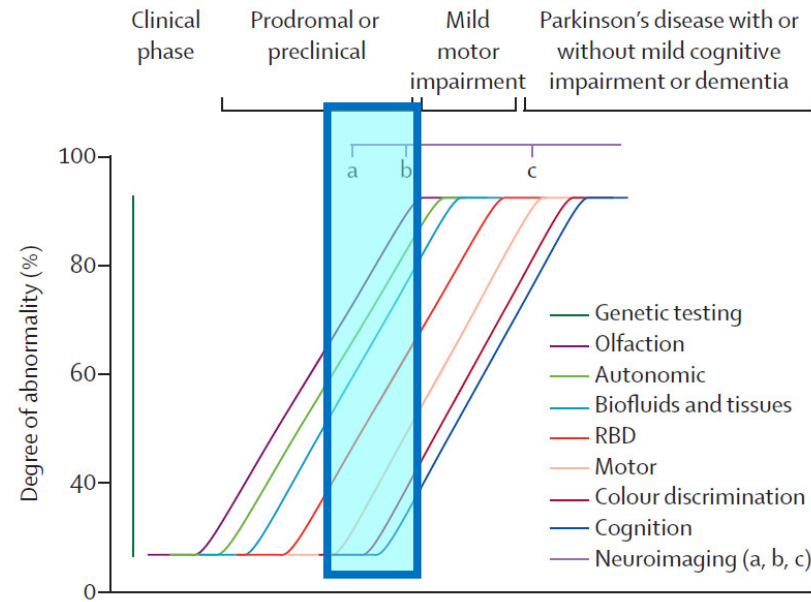




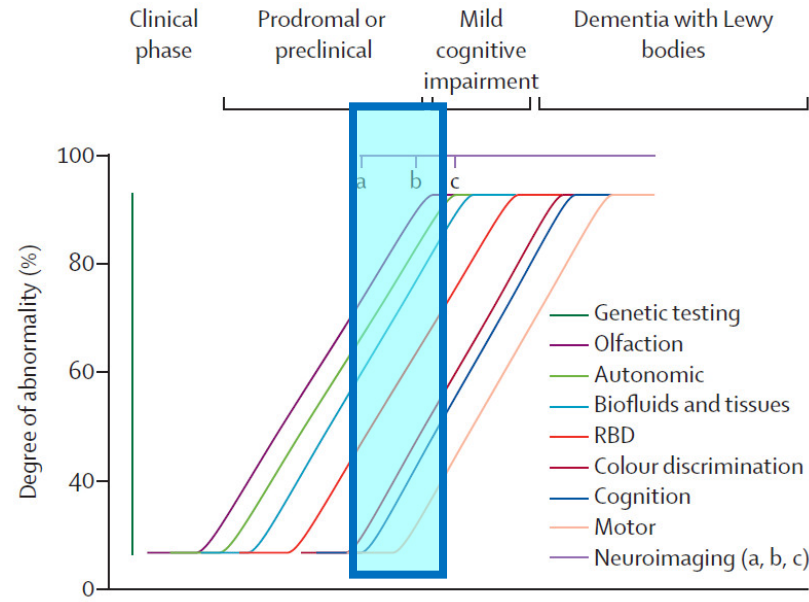


Neurodegenerative Diseases begin years before symptoms

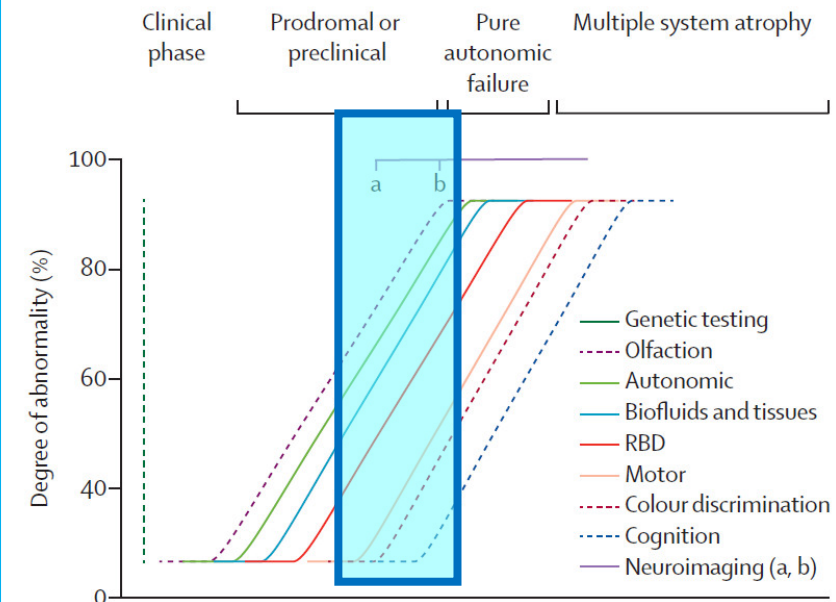
Parkinson Disease



Dementia with Lewy Bodies



Multiple System Atrophy



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REM Sleep Behavior Disorder (RBD)

- “Acting out of dreams” – fighting, screaming
- ~6-8% per year are diagnosed with synucleinopathy: Parkinson Disease (PD), dementia with Lewy bodies (DLB), Multiple system atrophy (MSA)
- RBD in most cases represents a *preclinical* or *prodromal* synucleinopathy → opportunity for intervention

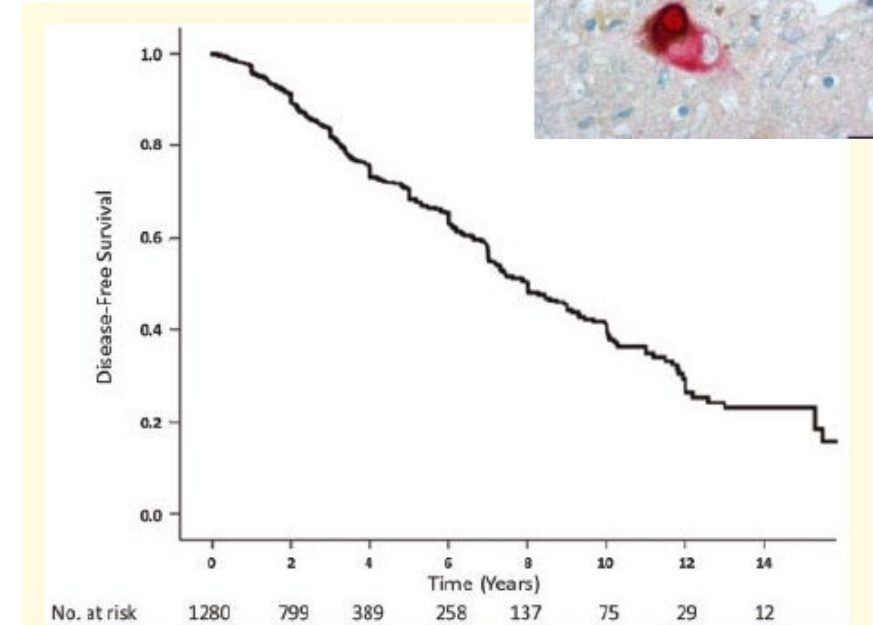
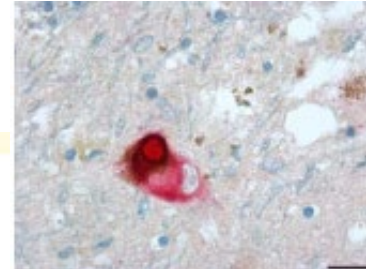


Figure 1 Kaplan-Meier plot of disease-free survival (i.e. free of parkinsonism or dementia) among patients with iRBD.



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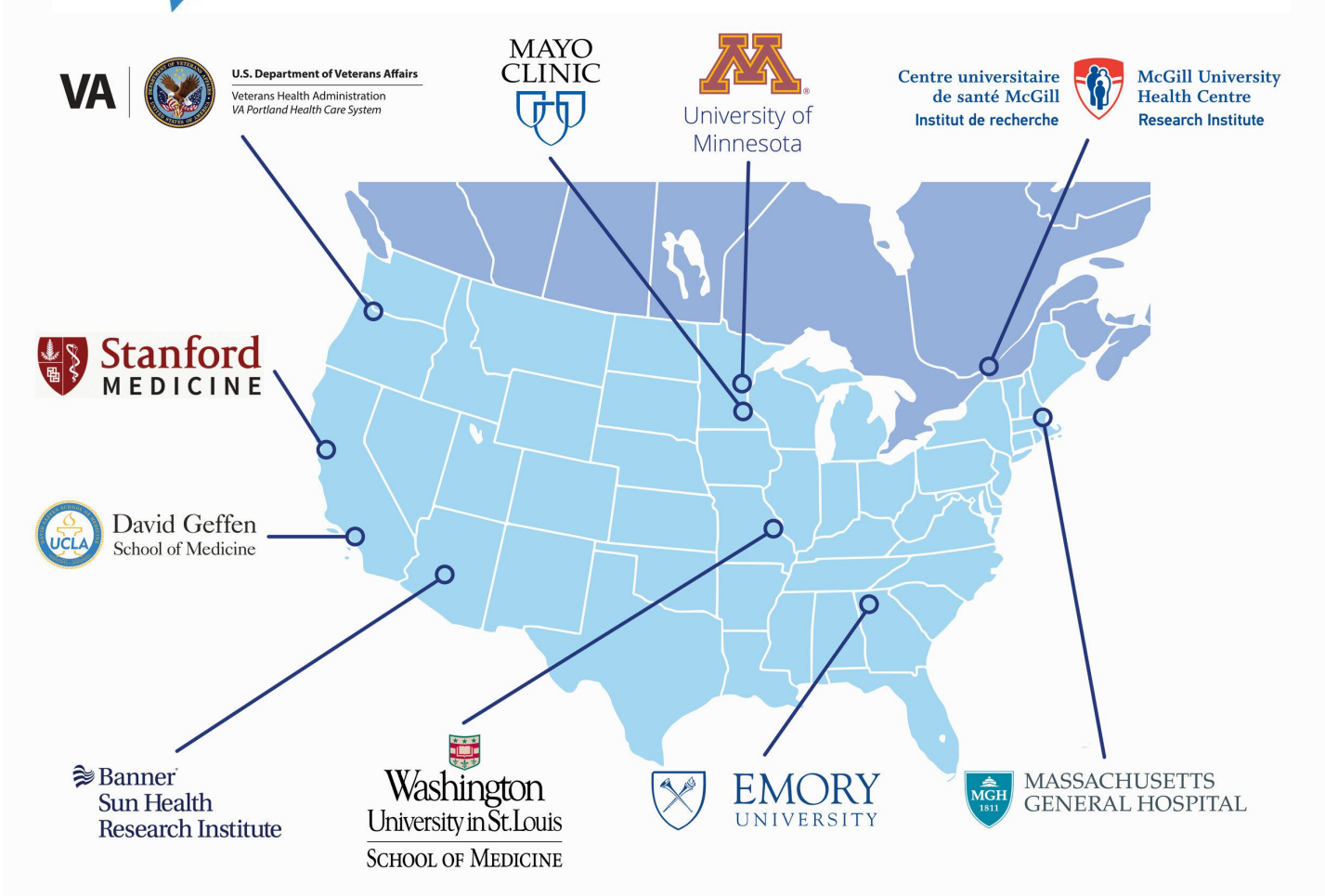
Boeve BF et al. *Mov Disord.* 2001; 16(4): 622-630.

Boeve BF et al. *Sleep Med.* 2013 Aug;14(8):754-62

Postuma et al, *Brain* 2019

NAPS CONSORTIUM

For REM Sleep Behavior Disorder



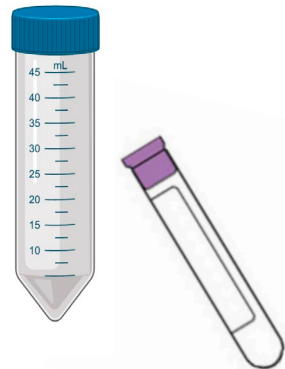
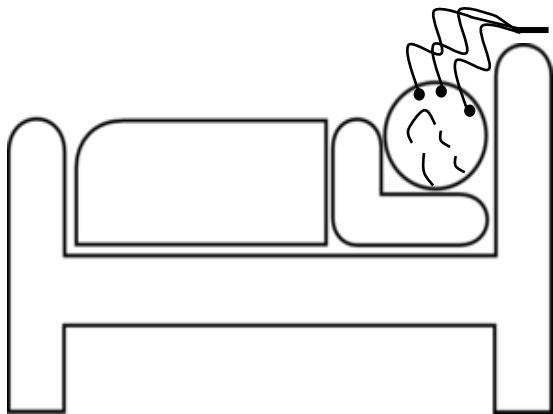
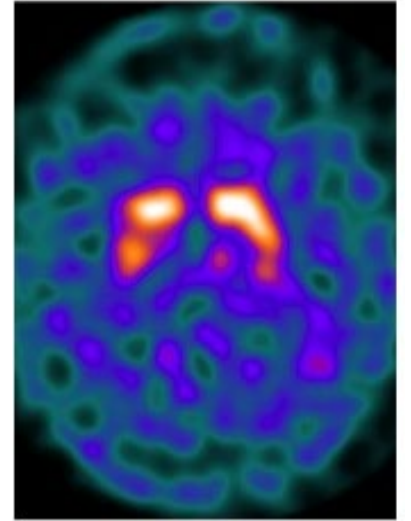
naps-rbd.org

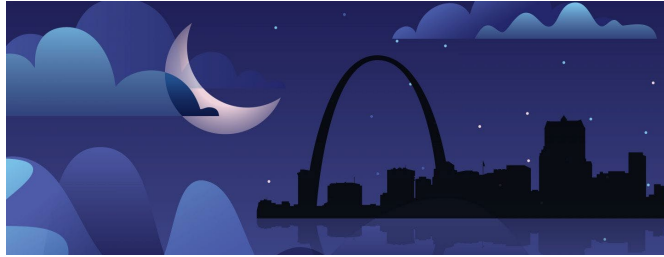
[Clinicaltrials.gov NCT03623672](https://clinicaltrials.gov/ct2/show/study/NCT03623672)

NIH R34AG056639; U19AG071754

North American Prodromal Synucleinopathy (NAPS) Consortium goals

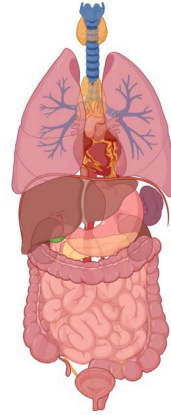
- Prepare for neuroprotective clinical trials in synucleinopathies
- Trial-ready cohort of >300 patients with RBD
- Longitudinal comprehensive assessment
- Biomarker development for synucleinopathies



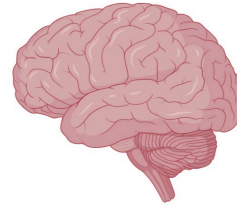


cobras.wustl.edu

Internal medicine



Neurology
Neurosurgery
Psychiatry



Anesthesiology

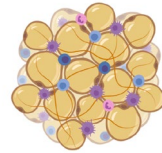


Obstetrics

Pediatrics
Child neurology



Metabolism



Ageing



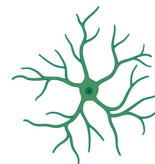
Neuroscience



Clinical trials
Implementation &
dissemination



Basic Science



Summary

- Neurodegenerative diseases begin years prior to symptoms → window of opportunity for treatment and prevention
 - Sleep disruption & Alzheimer disease
 - REM sleep behavior disorder (RBD) and synucleinopathies (Parkinson Disease, dementia with Lewy bodies, and multiple system atrophy)
- Sleep is a potential marker of neurodegenerative disease
- Sleep is also a potential target for intervention to impact neurodegenerative disease mechanisms
- Translational work at WashU on sleep-AD has laid the groundwork for clinical trials

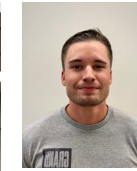


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Thank you!

- NIH:
 - KL2
 - Loan repayment program
 - K23-NS089922
 - R34-AG056639
 - R01-AG059507
 - RF1-AG061776
 - U19-AG07175
 - R01-DK115400 (Co-I)
 - R01-AG068579-02S1
 - R01-AG057901 (Co-I)
- Barbara Burton & Robert Morriss III Chair
- Centene/PMI
- American Sleep Medicine Foundation



- **The Feldman Family**, In memory of the late Dr. Robert A. Feldman, MD
- **Ms. Cynthia Cummings**, WashU Physical Therapy '67, In memory of her father
- **Dr. David and Tracy Holtzman**
- **The Knight Alzheimer's Disease Research Center**
- **Departments of Neurology and Anesthesiology**



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