



Lifestyle ROI

# SLEEP AND ALZHEIMER'S DISEASE IN DOWN SYNDROME



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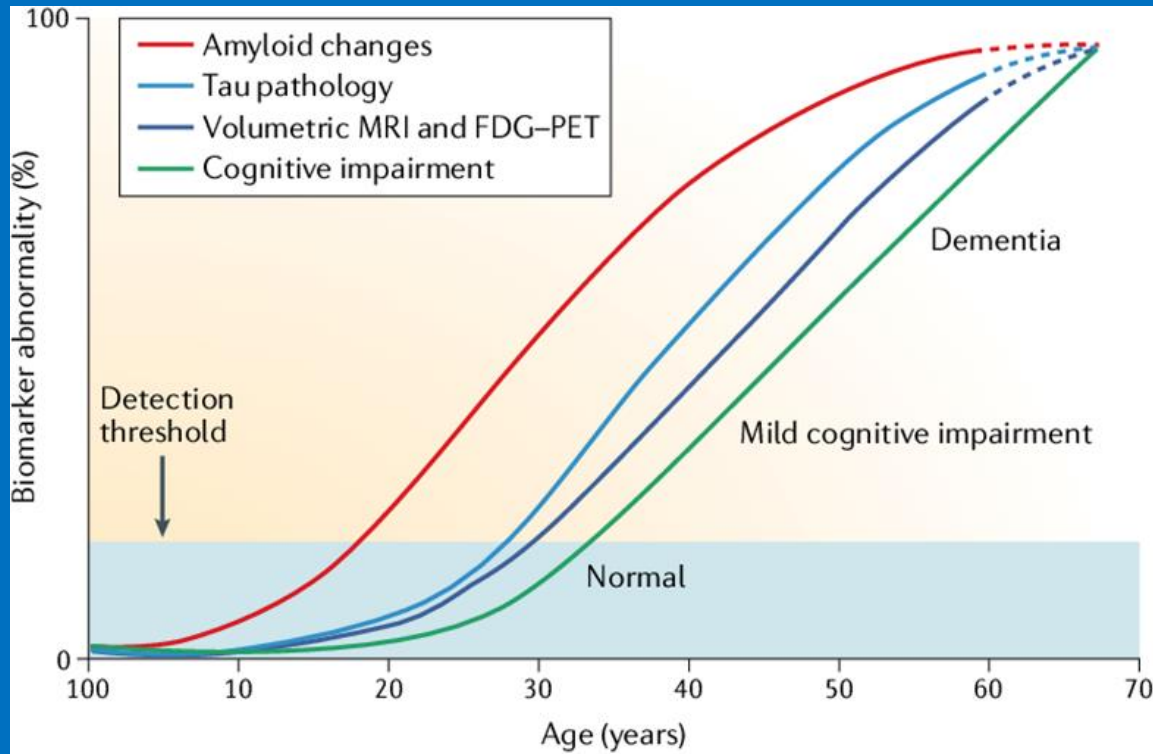
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ALZHEIMER'S BIOMARKER CONSORTIUM- DOWN SYNDROME

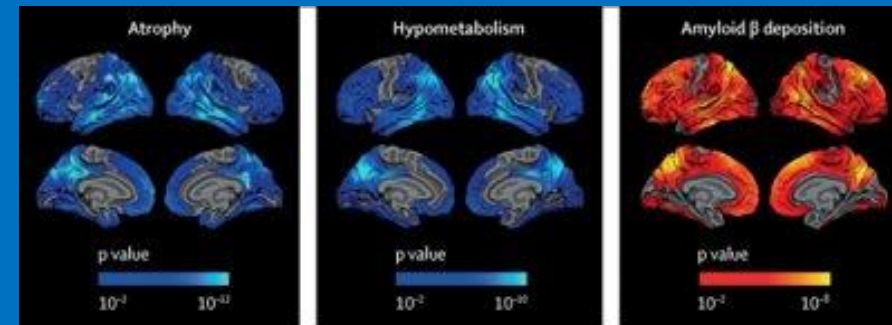


# ALZHEIMER'S DISEASE (AD) AND DOWN SYNDROME (DS)



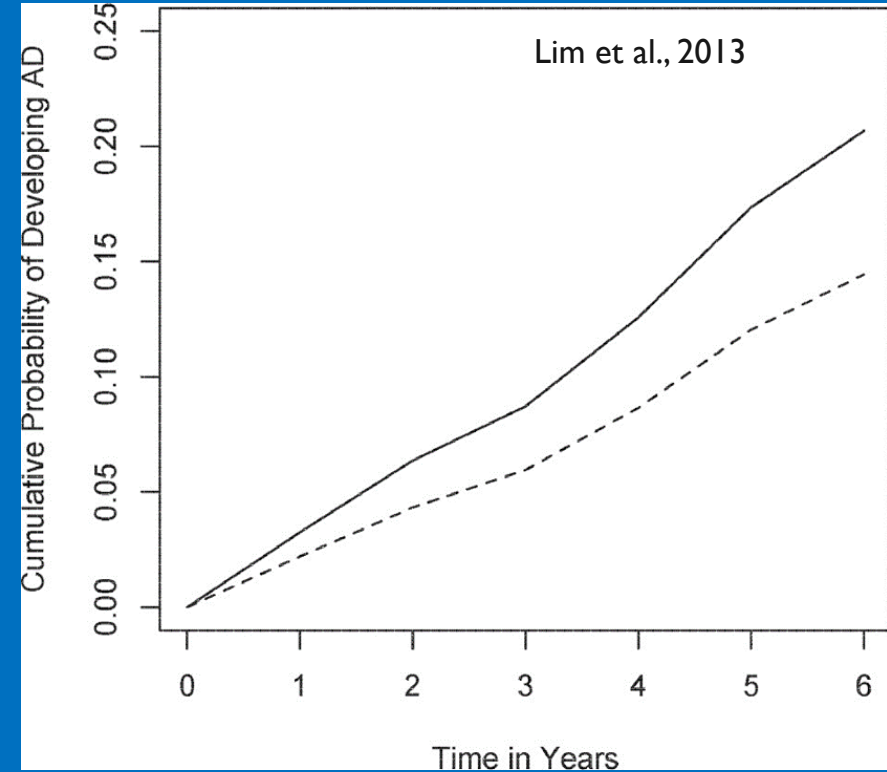
Fortea et al., 2020; Lao et al., 2017; Zammit et al., 2020; Head & Lott, 2019

- $A\beta$  plagues by age 40 yrs (Fortea et al., 2020; Lao et al., 2017; Zammit et al., 2021)
- Variability in age of onset
- AD dementia: late 40s-70s (Holland et al., 2000; Lai et al., 1989; Tyrrell et al., 2001)



# SLEEP AND AD OUTSIDE OF DS

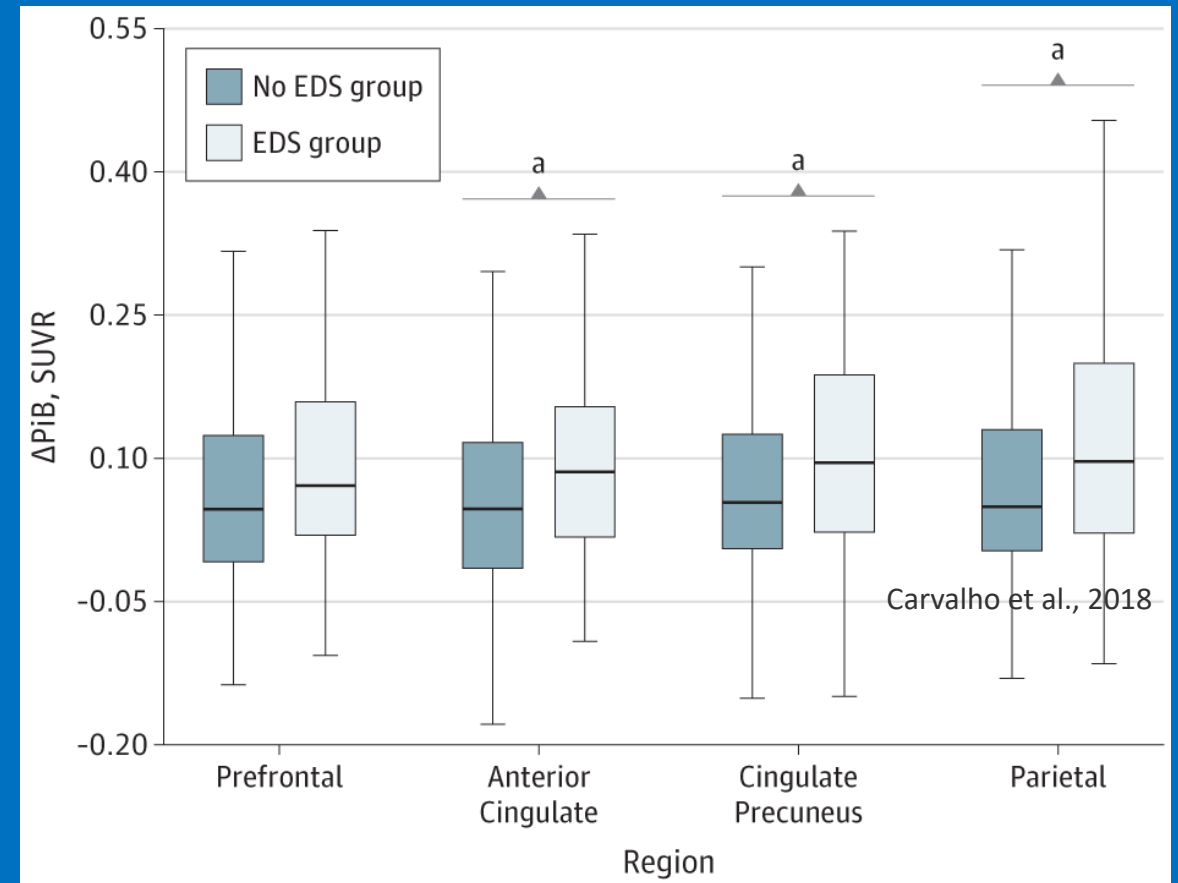
- Evidence from other AD populations of link between sleep and AD
- Sleep alternations precede diagnosis of AD dementia and is linked to early cognitive declines (Lim et al. 2013; Xu et al., 2011)



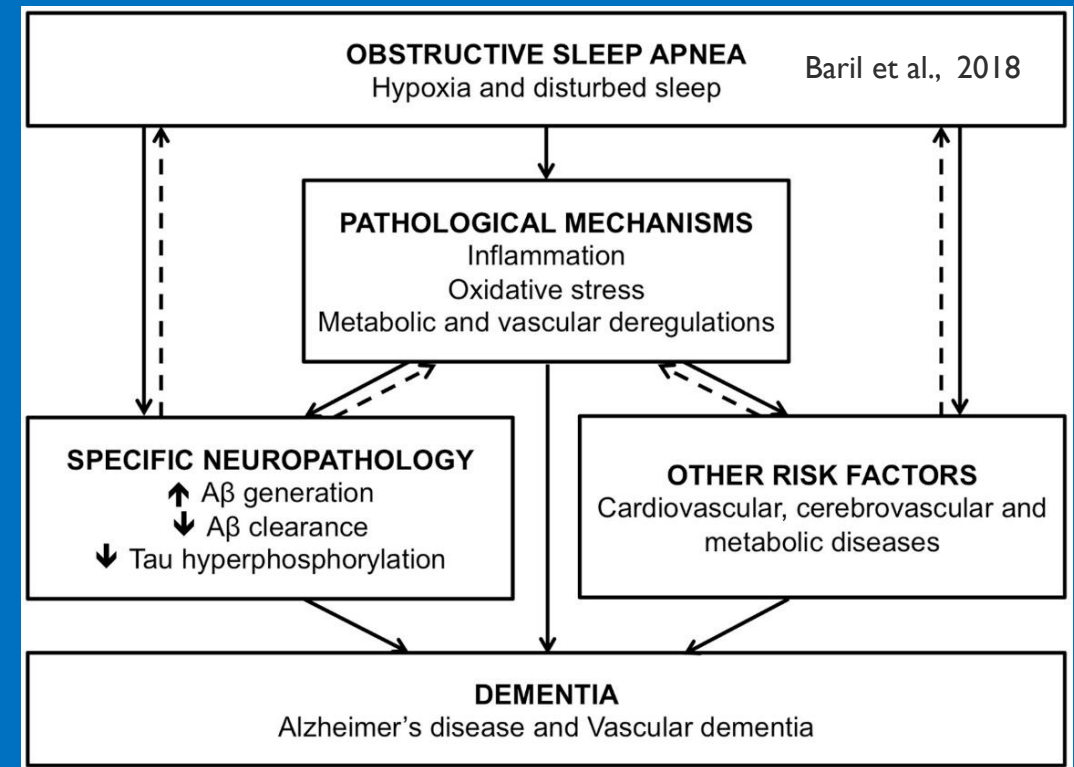
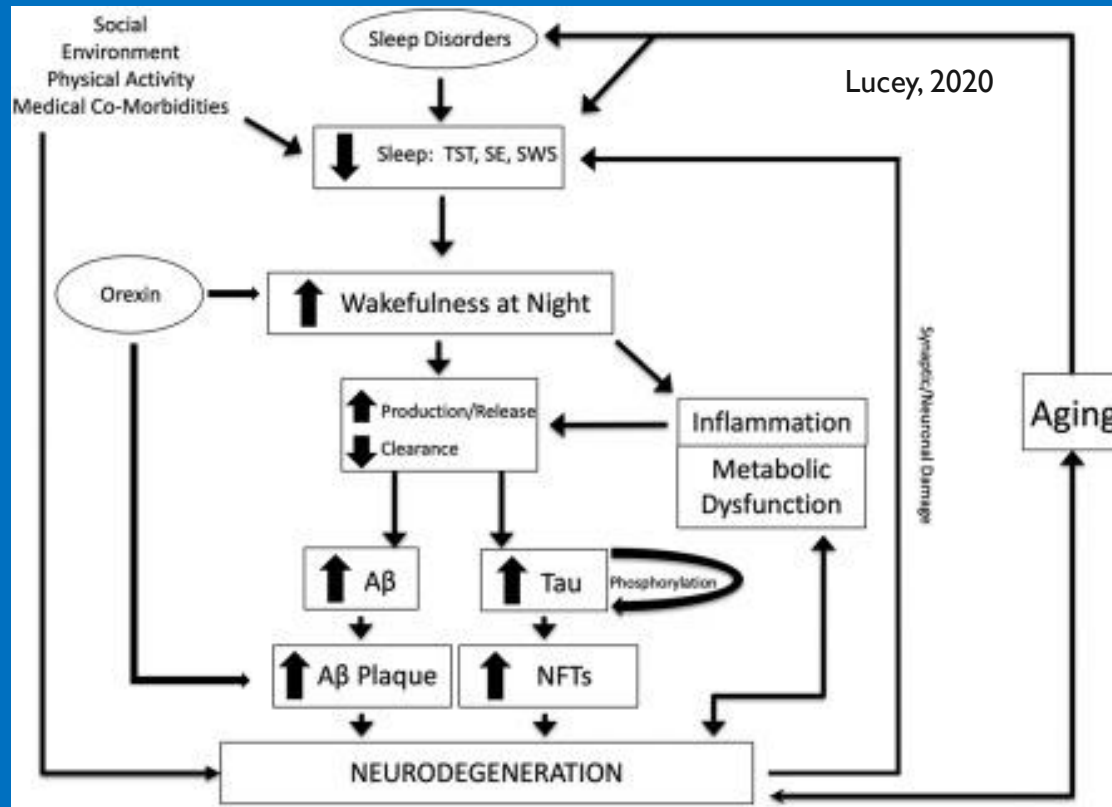
Expected risk of AD. The model predicted risk of AD for two hypothetical average participants with high (Solid line: 90<sup>th</sup> percentile;  $k_{RA} = 0.036$ ) and low (Dotted line: 10<sup>th</sup> percentile;  $k_{RA} = 0.021$ ) levels of sleep fragmentation.

# SLEEP AND AD OUTSIDE OF DS

- Evidence from both autosomal dominant and sporadic late onset AD of link between sleep and AD
- Sleep alterations associated AD pathology such as CSF and PET A $\beta$  and tau (e.g., Spira et al., 2013; Lucey et al., 2019; Mander et al. 2015)



# SLEEP DURATION AND DISRUPTIONS AND AD



# DISRUPTED SLEEP IN PEOPLE WITH DS

- Length of nighttime awakenings (LOA) associated with worse EF, memory, and motor control and planning in non-demented adults with DS
- LOA positively associated striatal PET A $\beta$  in non-demented adults with DS

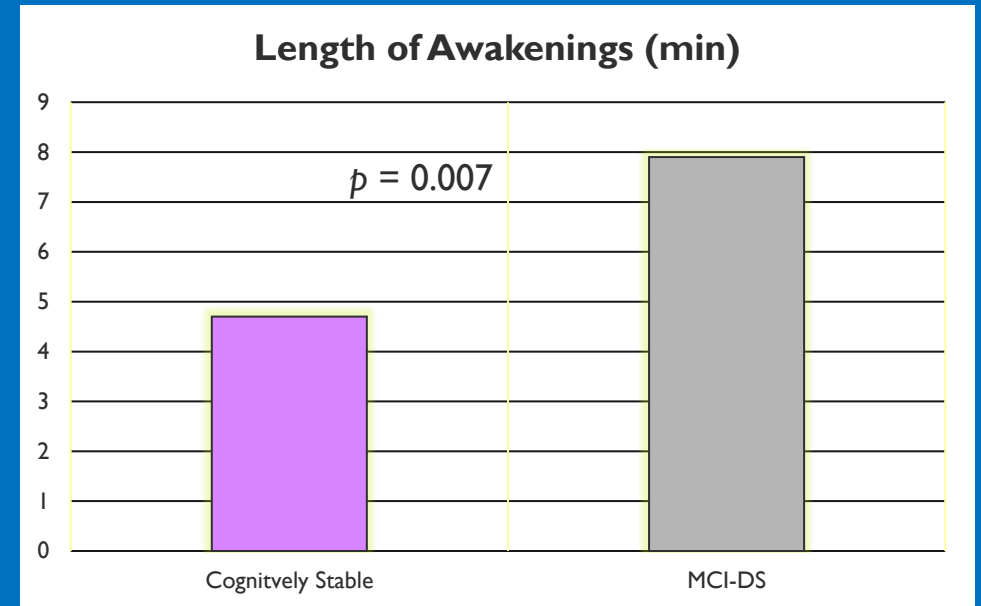
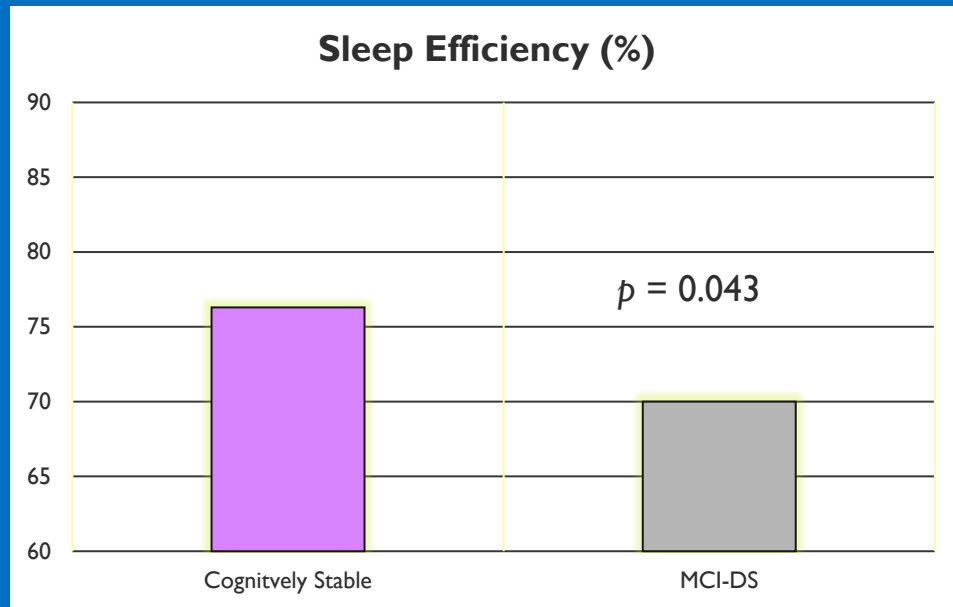


Domain	Measure	WASO	SE	NOA	LOA
Working memory	Free & Cued	-.283	.256+	.094	-.259
	Cued Recall Intrusions	.239	-.280	.049	<b>.291*</b>
	Rivermead	.073	-.132	.120	.156
	Digit Span Forward	-.004	.074	-.171	-.066
Executive Functioning	Digit Span backward	.048	.086	.286+	-.154
	Cat & Dog	.074	-.153	.009	<b>.358*</b>
Motor Planning & Control	Purdue Pegboard	-.179	.198	.038	<b>-.302*</b>
PET Amyloid- $\beta$	Striatum SUVR	.012	-.030	-.115	<b>.323*</b>

Cody et al., 220, Neurobiology of Aging



# SLEEP DISRUPTIONS AND AD IN PEOPLE WITH DS

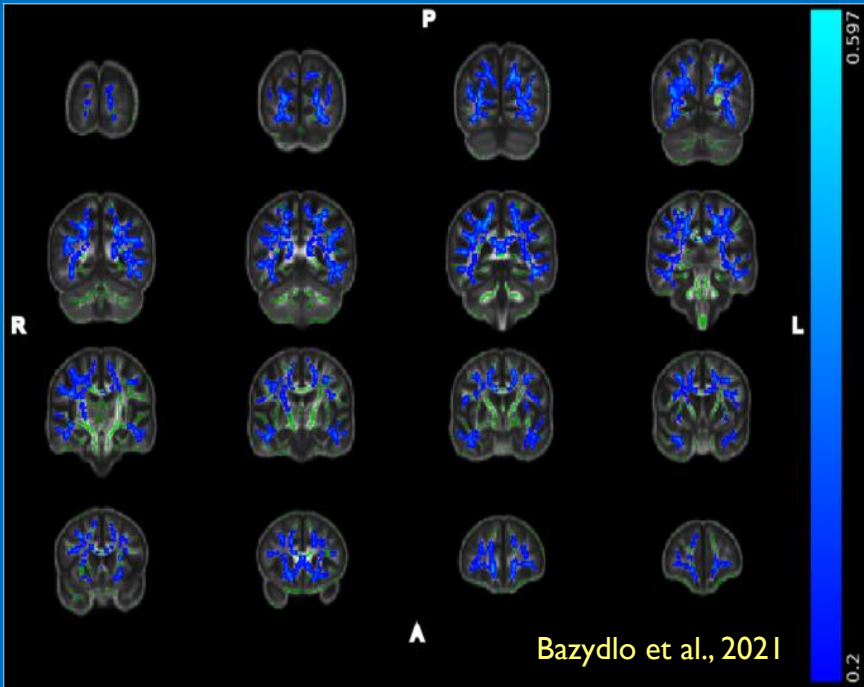


Cody et al., 2020

- Averages of other sleep indices
  - Total Sleep Time: 6.8 hours ( $SD = 1.1$ )
  - Wake After Sleep Onset: 113.4 minutes ( $SD = 41.2$ )
  - Number of Awakenings: 23.3 ( $SD = 8.1$ )

# SLEEP AND WHITE MATTER IN PEOPLE WITH DS

- White matter integrity linked to episodic memory (Bazydlo et al., 2021)



Fleming et al., 2021		TST <sup>1,2</sup>	WASO <sup>1,2</sup>	SE <sup>1,2</sup>	NOA <sup>1,2</sup>	LOA <sup>1,2</sup>	MI <sup>1,2</sup>	SFI <sup>1,2</sup>	OSA <sup>1</sup>
Superior longitudinal fasciculus, Left FA	Corr.	.233	-.240	.323	-.356	-.206	-.307	-.284	-.151
Superior longitudinal fasciculus, Right FA	Corr.	.135	-.220	.279	-.238	-.264	-.291	-.193	-.190
Inferior longitudinal fasciculus Left, FA	Corr.	.295	-.204	.328	.027	<b>-.425*</b>	-.317	-.210	-.229
Inferior longitudinal fasciculus, Right FA	Corr.	.279	-.280	<b>.387*</b>	.081	<b>-.614*</b>	<b>-.430*</b>	-.323	<b>-.373*</b>
Superior longitudinal fasciculus, Left MD	Corr.	<b>-.398*</b>	.131	-.216	.222	.053	.219	.203	-.111
Superior longitudinal fasciculus, Right MD	Corr.	-.201	.007	-.092	.003	.124	.130	.064	.213
Inferior longitudinal fasciculus, Left MD	Corr.	-.025	-.243	.224	-.218	-.196	-.288	-.313	-.054
Inferior longitudinal fasciculus, Right MD	Corr.	-.195	-.092	-.021	-.255	.167	.096	.034	.266

Note. TST = total sleep time; WASO = wake after sleep onset; SE = sleep efficiency; NOA = number of awakenings; LOA = length of awakenings; MI = movement index; SFI = sleep fragmentation index; OSA = obstructive sleep apnea \*p < .05. <sup>1</sup> = controlling for age; <sup>2</sup> = controlling for # valid nights of actigraphy data.

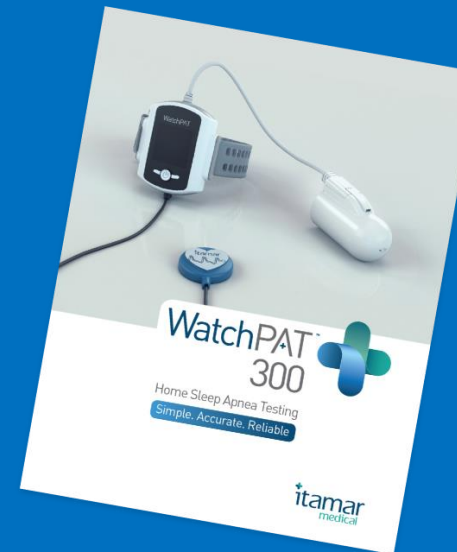


# SLEEP DISORDERED BREATHING - OSA

- OSA in 30-50% of children (Hill et al., 2020; Stores & Stores, 2013; Tietze et al., 2012)
- 50 to 90% in adults with DS based on informant report (Marcus et al., 1991) and objective measures (Resta et al., 2003; Trois et al., 2009)

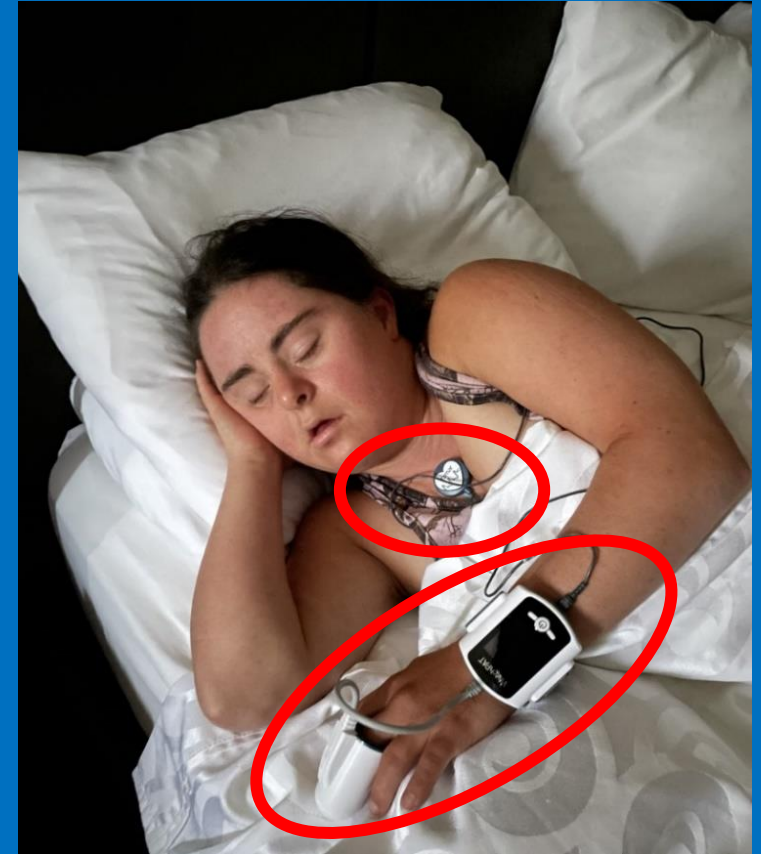


David Plante, MD



# SLEEP DISORDERED BREATHING

- ABC-DS Caregiver -reported sleep apnea (baseline UOI; N = 289)
  - 35% diagnosed with OSA
  - 62% actively being treated, often partial compliance
- WatchPAT 300
  - 55 consented
  - 49 (89%) completed with valid data
  - 6 (11%) could not complete
    - Dementia, took off finger probe, failure turning on



Fleming et al., in prep

# SLEEP DISORDERED BREATHING

## Apnea Hypopnea Index (AHI)

Severity	Definition	N (%)
None/Minimal	< 5 per hr	4 (8.5%)
Mild	$\geq 5$ but < 15 per hr	14 (29.8%)
Moderate	$\geq 15$ but < 30 per hr	11 (23.4%)
Severe	$\geq 30$ per hr	12 (25.5%)

AHI = number of apneas or hypopneas recorded during the study per hour of sleep

	M (SD)	Range
AHI	22.71 (20.37)	1.90-98.10
Percent of REM (%)	22.70 (7.80)	5.70-39.60
Latency to REM (mins)	106.93 (49.52)	37.00-239.00
Mean Oxygen Saturation (%)	93.90 (2.72)	81.00-98.00



Fleming et al., 2022

# SLEEP DISORDERED BREATHING

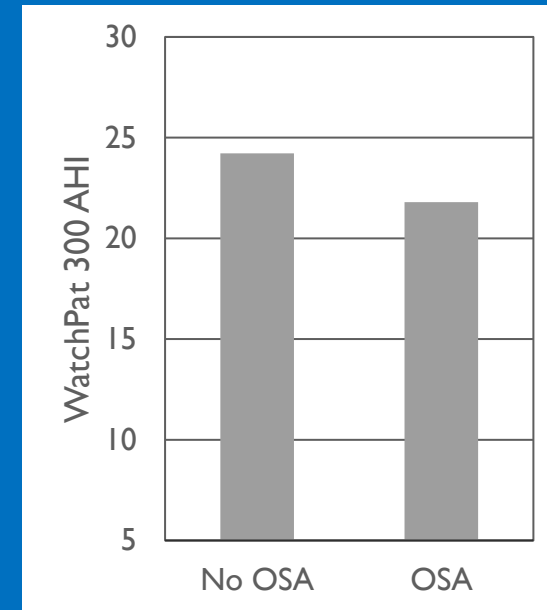


	No reported OSA	Reported OSA
WatchPAT No OSA	24%	0%
WatchPAT OSA	76%	100%

$$\chi^2 (1,41) = 5.28, p = .022$$

	No reported OSA	Reported OSA
AHI None/Minimal	24%	0%
AHI Mild	24%	45%
AHI Moderate	29%	25%
AHI Severe	24%	30%
	<b>100%</b>	<b>100%</b>

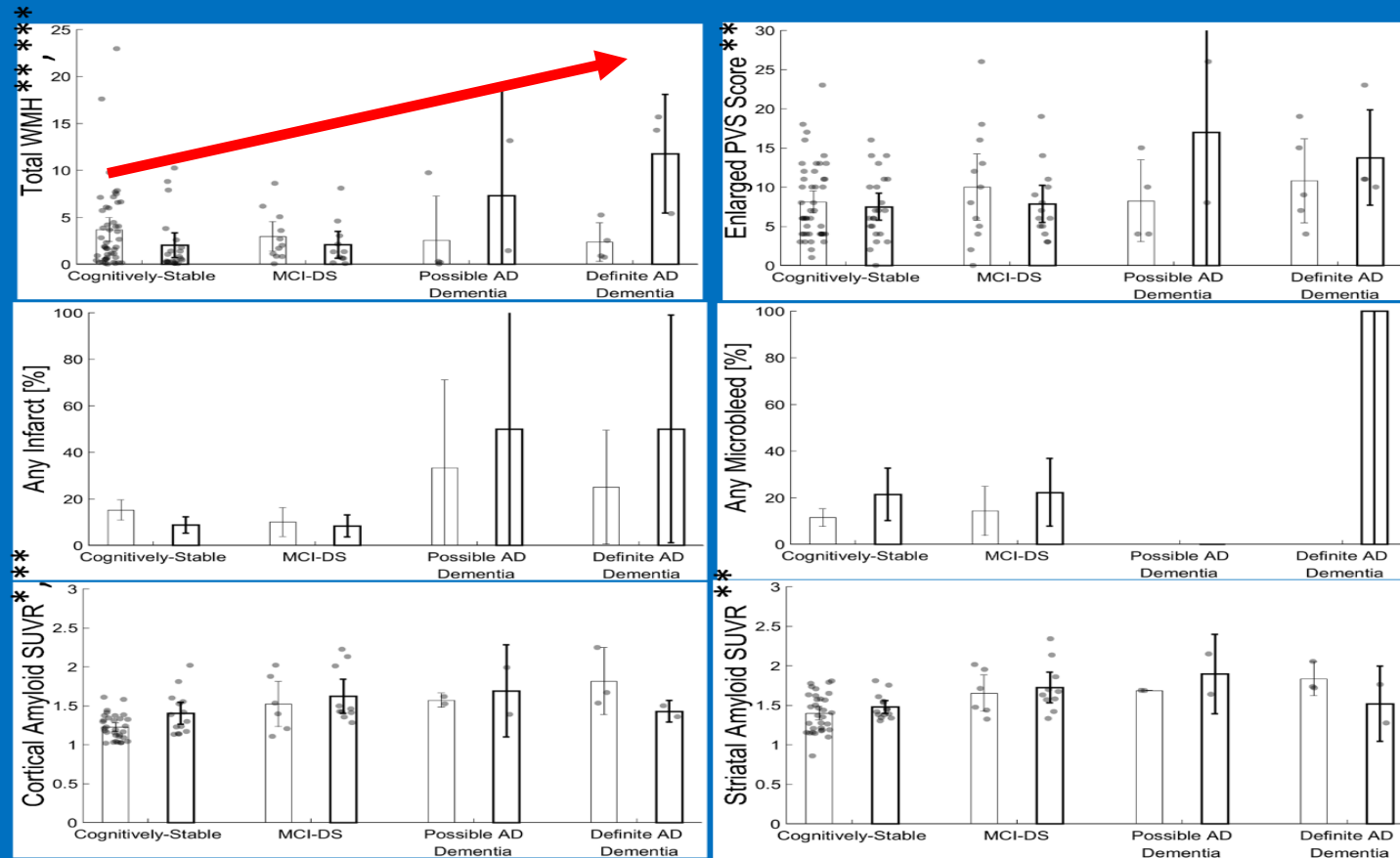
$$\chi^2 (3,39) = 6.12, p = .106$$



$$t (41) = 0.43, p = .689$$

Fleming et al., 2022

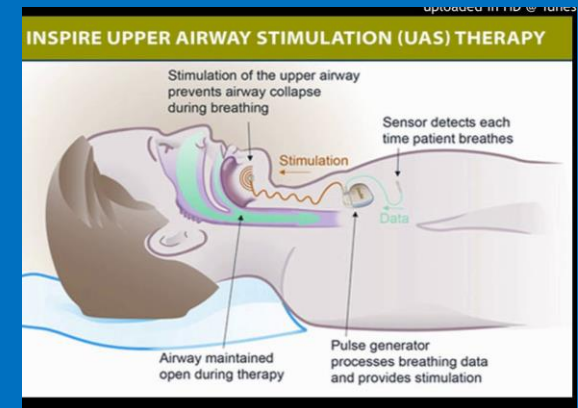
# SLEEP DISORDERED BREATHING AND WHM



Lao et al., 2022

# POTENTIAL TREATMENT CONSIDERATIONS

- Regular Screenings for OSA
- Treatment of OSA
  - Positive airway pressure devices
    - In middle-aged adults without Down syndrome, linked to reduction in CSF A $\beta$  and tau (e.g., Ju et al., 2019)
    - Compliance can be difficult (e.g., Simpson et al., 2018)
    - But, with education and support good compliance has been reported in adults with DS (Gimenez et al., 2022)
  - Other treatment options
    - Hypoglossal nerve stimulator





# ACKNOWLEDGEMENTS

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ALZHEIMER'S BIOMARKER CONSORTIUM- DOWN SYNDROME

