

Timing of sleep-disordered breathing and Alzheimer’s disease –Apnoeas in REM versus non-REM sleep

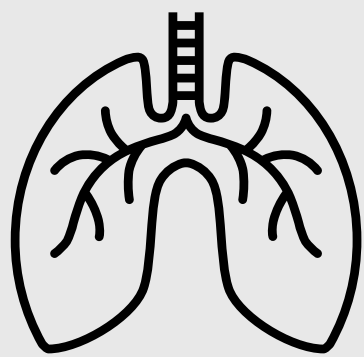


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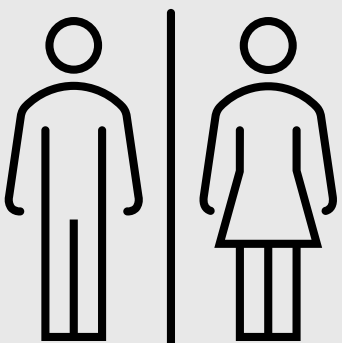
BACKGROUND

Sleep is considered a potentially modifiable risk factor for dementia. Sleep apnoea, a common respiratory sleep disorder, has been shown to augment Alzheimer’s disease (AD) pathology (e.g. β -amyloid and tau).



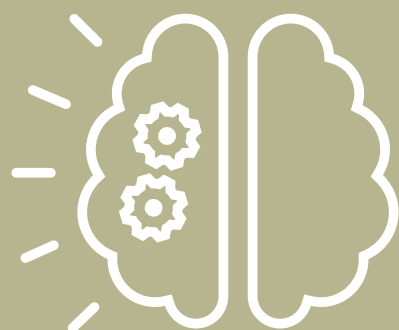
Apnoeas can occur in different sleep stages. Apnoeas occurring in rapid eye movement (REM) versus non-REM (NREM) sleep may have differential mechanisms of accelerating neurodegenerative diseases and disrupting sleep and cognition performance.

Females are more likely to develop AD whereas males are more likely to have sleep apnoea. AD and the menopause may contribute to a different apnoea REM and NREM proportions between the sexes.



OBJECTIVE

- 1) To examine if there is a difference in apnoea proportion across REM and NREM between people with and without AD.
- 2) To inspect sex differences in apnoea proportion within and between AD and non-AD
- 3) Determining if apnoeas proportion predict cognitive performance



METHOD

Study design

An exploratory interim secondary analysis of the Sleep Apnoea and Memory study which is determining prevalence of sleep apnoea in memory clinics. Participants undergo one night using a respiratory polygraphy (WatchPAT300). An automated algorithm (zzzPAT) determined sleep architecture via 4 different channels including pulse rate, SpO2 levels, actigraphy and peripheral arterial tone (PAT) amplitude.

Participant criteria

AD → clinically probable AD
Non-AD → No evidence of AD
Cognitive Z score → combination of Moca and ACE scores

REM and NREM apnoea proportion

ODI3% → quantity of ODI3% per hour
$$\frac{\text{NREM ODI3\%}}{(\text{NREM ODI3\%} + \text{REM ODI3\%})}$$

Regression models

Objective 1) REM and NREM ODI3% Proportion ~ AD diagnosis
Objective 2) REM and NREM ODI3% Proportion ~ AD diagnosis * sex + age
Objective 3) Cognitive z-scores ~ REM and NREM ODI3% proportion + overall ODI3% + sex + age + AD diagnosis

RESULTS

25 participant with AD and 22 non- AD participants had available data to compare apnoea proportion.

Linear Regression Model (n = 47)

Overall, there were more apnoeas in NREM than REM in AD patients (AD mean $\pm$ SE = 0.49 ± 0.05 , non-AD mean $\pm$ SE = 0.34 ± 0.04 , $R^2 = 12.21\%$, $p = 0.014$)

AD diagnosis in females has a higher proportion of NREM apnoeas when age is controlled ($R^2 = 27.39\%$, $p = 0.033$). A descriptive model using sex as an interaction suggests AD females are the driver of higher NREM apnoeas in AD ($R^2 = 25.43\%$, $p = 0.012$, **Figure 1**)

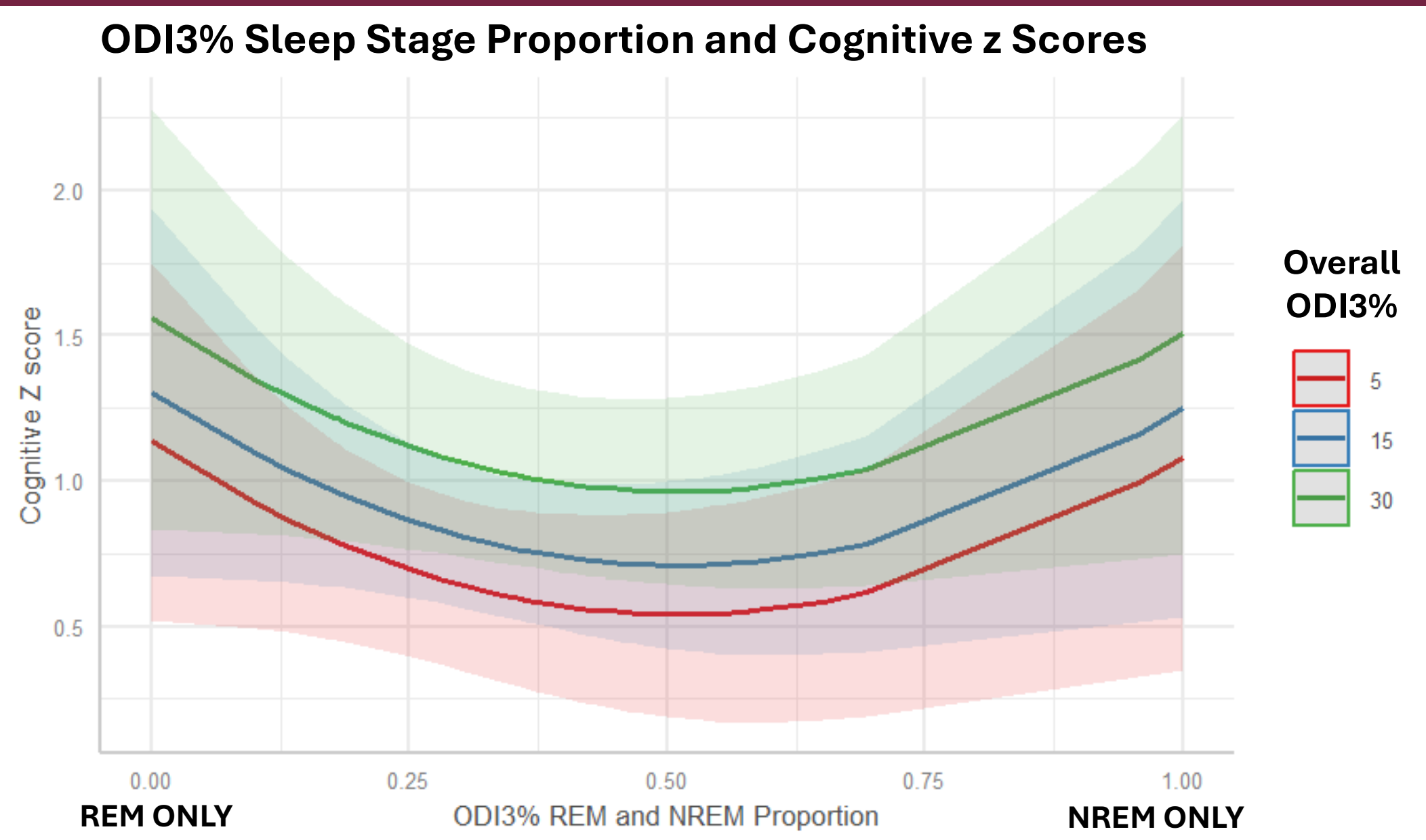


Figure 2. ODI3% REM/NREM proportion predicting cognitive z scores

Aetiology	Age	BMI	ODI3%
	Mean/SD	Mean/SD	Mean /SD
Non-AD	68.9/9.7	25.5 /4.8	7.9 /6.2
AD	73.9 /8.7	24.6 /4.6	11.1 /12.3

Aetiology	Age	BMI	ODI3%
	Mean/SD	Mean/SD	Mean/SD
Non-AD	64.5/10.7	28.4 /4.4	16.4/16.1
AD	68.9/6.3	26.8/3.1	12.0 /10.8

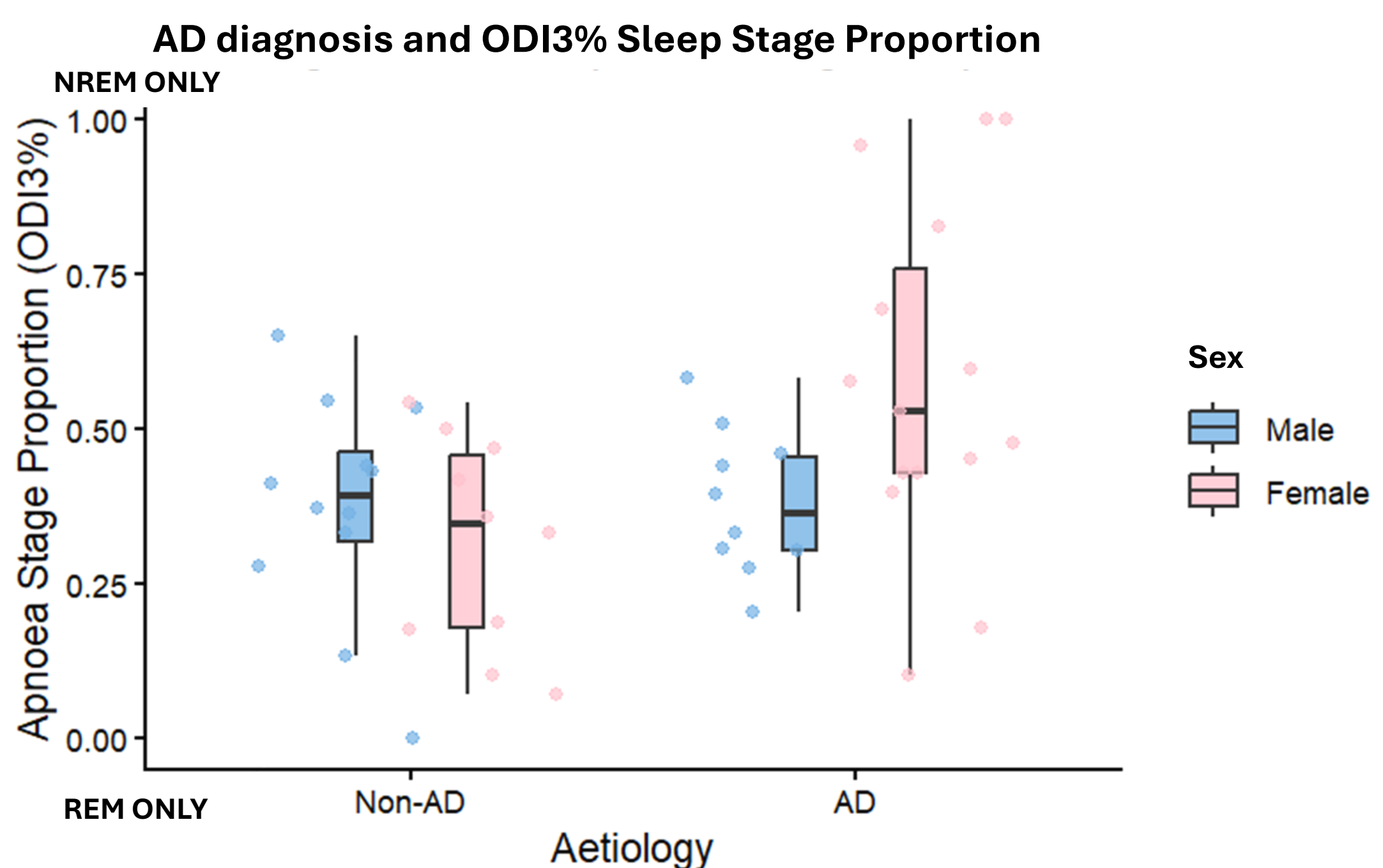


Figure 1. AD diagnosis predicting ODI3% REM/NREM proportion split by sex

Quadratic Regression Model (n = 34)

There is a U-shaped relationship ($x^2 = -2.76$, $p = 0.02$, $x = -2.77$, $p = 0.032$) with a turning point of 0.49 suggesting an equal distribution of REM and NREM apnoeas predicts lower cognitive scores ($R^2 = 77.99\%$, $p < 0.001$, **Figure 2**). Explanations are unclear but there may be a link to rate of awakenings and oxygen saturation mean as both peaking and dipping at 0.49 ODI3% REM/NREM proportion.

DISCUSSION

- 1) AD participants have significantly higher proportion of NREM apnoeas than non-AD participants.
- 2) NREM apnoeas are more prominent in women with AD than men with or without AD and women without AD.
- 3) Explanations are unclear but hormonal changes at menopause may be a factor
- 4) Neuroplasticity may be more dysfunctional when both REM and NREM are disrupted as neither memory consolidation or stabilisation of memories can occur as hypothesised by ‘The Active System Consolidation Hypothesis’.
- 5) Data collection is still underway, and future research will focus on the differences of apnoea REM/NREM proportions across different neurodegenerative aetiologies, and explanations for the impact of NREM and REM desaturations on cognition such as the relative number of awakenings and overall oxygen saturation.

CONCLUSION

NREM apnoeas may represent a sex-specific vulnerability to AD or an effect of the disease.