

Greater hypoxemia during REM sleep is linked to decreased basal forebrain volume in older adults who are ptau217 positive

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Introduction

Rodent studies indicate that intermittent nocturnal hypoxemia accelerates basal forebrain neurodegeneration¹. Human evidence linking obstructive sleep apnea (OSA) to basal forebrain structure is limited, and stage-specific hypoxemia (rapid eye movement [REM] vs. non-REM) may be critical. REM-predominant OSA often yields deeper desaturations, potentially interacting with Alzheimer's pathology.

Aims

To examine whether stage-specific hypoxemia is associated with basal forebrain volume within pTau217 positive and negative older adults.

Materials and methods

- Participants aged 50+ were recruited from the Healthy Brain Ageing Clinic
- Neuropsychological assessment, fasting blood test, neuroimaging, and polysomnography
- Plasma p-tau217 was used to categorise negative or positive status using validated cut-offs
- REM oxygen desaturation index 3% (ODI) was the primary hypoxemia metric, with non-REM ODI examined secondarily.

Results

Table 1. Descriptives of the whole sample and the p-tau217 negative and positive groups

	Whole sample	p-tau217 negative	p-tau217 positive	p-value
N	148	119	29	
Age, years	67.7 ± 7.9	66.4 ± 7.5	73.2 ± 7.3	0.001**
Sex, no. female (%)^a	98 (66.2%)	77 (64.1%)	22 (72.4)	0.570
Education, years	14.7 ± 2.7	14.7 ± 2.7	14.6 ± 3.0	0.170
Body mass index^b	26.0 ± 5.5	26.3 ± 5.0	25.4 ± 6.9	0.726
MMSE^c	29.0 ± 2.0	30.0 ± 1.0	28.0 ± 2.3	0.001**
GDS-15^c	3.0 ± 5.0	3.0 ± 5.0	2.0 ± 2.0	0.033*
CIRS-G	6.4 ± 3.4	6.2 ± 3.4	6.0 ± 2.1	0.790
Alcohol, units/week^c	2.8 ± 8.0	3.0 ± 9.0	0.0 ± 2.0	0.002**
Cognitive status, with MCI (%)^a	61 (41.2%)	39 (32.8%)	22 (75.9%)	0.001**

*p<0.05, **p<0.01

^aChi-square test was conducted. ^bMedian and interquartile range (IQR) are reported; values were log-transformed prior to an independent t-test. ^cMedian and interquartile range are reported; group comparisons were performed using the Wilcoxon rank-sum test.

MMSE = Mini-Mental State Examination; GDS-15 = geriatric depression scale – 15 items; CIRS-G = cumulative illness rating scale – geriatric version; MCI = mild cognitive impairment.

Ptau217 positive vs. negative

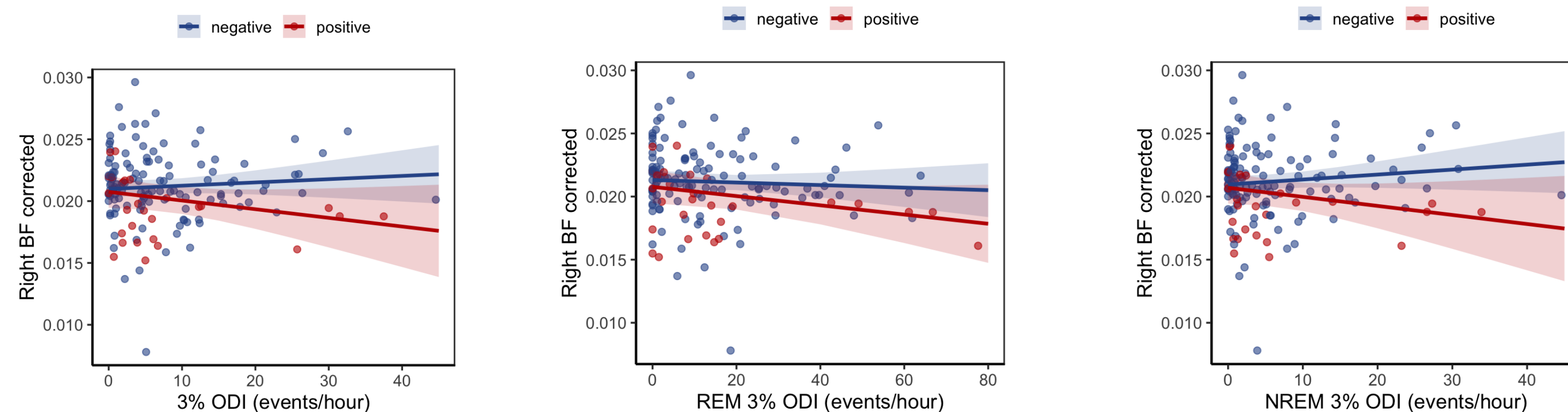


Table 2. P-tau positive associations

Predictor	β	p-value	q-value
Right BF volume ~ ODI TST	-0.324	0.012	0.032*
Left BF volume ~ ODI TST	-0.164	0.378	0.408
Right BF volume ~ ODI REM	-0.347	0.002	0.012*
Left BF volume ~ ODI REM	-0.292	0.165	0.248
Right BF volume ~ ODI NREM	-0.309	0.016	0.032*
Left BF volume ~ ODI NREM	-0.153	0.408	0.408

Abbreviations: β = standardised regression coefficient; SE = standard error; FDR = false-discovery rate; BF = basal forebrain; TST = total sleep time; REM = rapid eye movement sleep; NREM = non-rapid eye movement sleep; ODI = oxygen desaturation index

Table 3. P-tau negative associations

Predictor	β	p-value	q-value
Right BF volume ~ ODI TST	0.049	0.495	0.743
Left BF volume ~ ODI TST	0.023	0.772	0.772
Right BF volume ~ ODI REM	-0.072	0.414	0.743
Left BF volume ~ ODI REM	-0.059	0.493	0.743
Right BF volume ~ ODI NREM	0.089	0.240	0.743
Left BF volume ~ ODI NREM	0.035	0.656	0.772

Abbreviations: β = standardised regression coefficient; SE = standard error; FDR = false-discovery rate; BF = basal forebrain; TST = total sleep time; REM = rapid eye movement sleep; NREM = non-rapid eye movement sleep; ODI = oxygen desaturation index

Core findings

In p-tau positive participants:

- ODI is associated with right BF volume; the effect is the largest for ODI during REM sleep.
- ODI is not related to left BF volume.

In p-tau negative participants:

- ODI is not related to BF volume

Conclusion

- The relationship between ODI and BF is dependent on p-tau positivity.
- This is likely due to the heightened vulnerability of the BF in older adults who are p-tau positive.
- Critically, aligned with prior work, hypoxemia during REM appears to have a stronger effect on neurological alterations², than NREM.
- Next steps: assessing the longitudinal changes to BF to establish temporal association between ODI and BF

References

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