

Introduction

The basal forebrain is one of the earliest regions affected in Alzheimer's disease¹. Within the basal forebrain, the nucleus basalis of Meynert (NbM) provides the major cholinergic input to the neocortex and cortical activation during REM sleep². REM electroencephalography (EEG) slowing has been consistently observed in older adults with Alzheimer's disease and amnesic mild cognitive impairment (MCI)³.

Aims

We investigated associations between REM EEG slowing and NbM volume. We also investigated whether cognitive status, sex, or sleep apnea severity moderated this relationship.

Materials and methods

Participants: Adults aged ≥ 60 years with subjective cognitive impairment (SCI) or MCI.

Assessments: Neuropsychological, medical, overnight polysomnography, and magnetic resonance imaging.

Brain measures: Bilateral NbM and Ch1–3 volumes (corrected for intracranial volume).

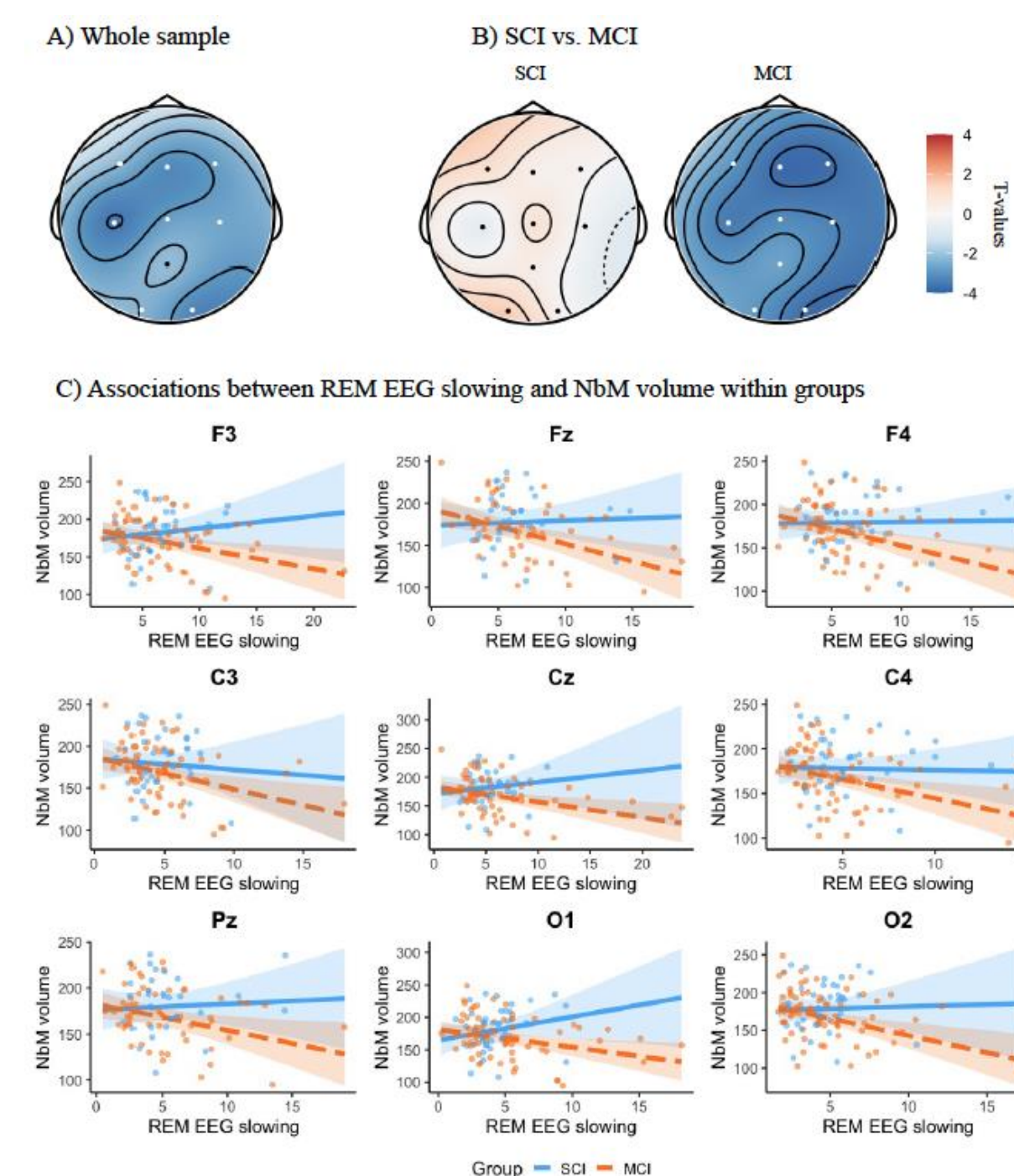
REM EEG slowing is the ratio of delta and theta ($< 8\text{Hz}$) to alpha, sigma, and beta bands ($8\text{--}32\text{Hz}$).

Results

Participant demographics	Whole sample	SCI	MCI	statistic	p-value
N	116	41	75		
Age, years	70.5 $\pm$ 6.1	68.1 $\pm$ 5.6	71.6 $\pm$ 6.0	-3.11	0.002**
Sex, no. female (%)	69 (59.5%)	26 (63.4%)	43 (57.3%)	0.19	0.660
Education, years	13.6 $\pm$ 3.1	13.4 $\pm$ 3.1	13.7 $\pm$ 3.1	-0.55	0.583
Alcohol, units/week^{a,b}	2.0 $\pm$ 7.0	7.0 $\pm$ 9.0	1.5 $\pm$ 5.5	2002	0.006*
Body Mass Index^a	25.9 $\pm$ 5.3	25.3 $\pm$ 4.3	26.0 $\pm$ 5.7	-0.73	0.468
Cumulative Illness Severity^a	5.0 $\pm$ 5.0	5.0 $\pm$ 4.3	5.0 $\pm$ 5.0	0.36	0.718
GDS-15^{a, b}	2.0 $\pm$ 3.0	2.0 $\pm$ 3.0	2.0 $\pm$ 3.0	2006	0.447
PSQI	7.1 $\pm$ 3.8	7.9 $\pm$ 4.1	6.7 $\pm$ 3.6	1.57	0.121
MMSE^{a, b}	29.0 $\pm$ 2.0	29.0 $\pm$ 1.0	29.0 $\pm$ 2.0	1708	0.087
Cognitive status, with MCI (%)	75 (64.7%)	-	-	-	-
Bilateral NbM volume	183.0 $\pm$ 31.5	183.4 $\pm$ 31.7	170.9 $\pm$ 31.3	2.03	0.046*
Bilateral Ch1-3 volume	131.4 $\pm$ 31.9	145.3 $\pm$ 36.5	124.4 $\pm$ 27.3	3.20	0.002**
OSA, with moderate or severe (%)	45 (38.8%)	18 (39.9%)	27 (36.0%)	0.40	0.525

* $p < 0.05$, ** $p < 0.01$. ^aMedian and interquartile range was reported. ^bWilcoxon rank sum test conducted. GDS-15 = geriatric depression scale-15 items; PSQI = Pittsburgh Sleep Quality Index; MMSE = mini-mental state examination; MCI = mild cognitive impairment; NbM = Nucleus basalis of Meynert; Ch1-3 = medial septal nucleus and the vertical and horizontal limb of the diagonal band of Broca; OSA = obstructive sleep apnea.

Associations between REM EEG slowing and NbM volume



Main analyses:

- REM EEG slowing predicted NbM volume after controlling for age, sex, OSA severity, after corrections for multiple comparisons.
- Cognitive status moderated the relationship, but the effect did not survive multiple comparisons.
- Post-hoc within-group analyses suggest that the relationship may be stronger in the MCI group.
- Sex and OSA severity did not moderate the relationship.

Specificity analyses:

- No significant associations between the non-REM EEG slowing ratio and NbM volume.
- No significant associations between the REM EEG slowing ratio and Ch1-3 volume.

Exploratory analyses:

- Higher NbM volume is associated with lower sleep latency and better learning and memory performance.

Core findings

- Greater REM EEG slowing predicted lower NbM volume.
- The relationship was stronger in the MCI group than in the SCI group.
- Higher NbM volume was associated with faster time to fall asleep.
- Higher NbM volume was associated with better learning and memory scores.

Conclusion

- Our findings were specific to REM sleep, as the same non-REM ratio was not significant.
- Findings were also specific to NbM, as REM EEG slowing was not linked to Ch1-3.
- Together with previous work⁴, REM EEG slowing may be a low-cost, scalable tool for detecting cholinergic dysfunction.
- Future work is underway to investigate whether REM EEG slowing may predict structural and functional cholinergic connectivity.

References

- Geula C. et al. Basal forebrain cholinergic system in the dementias: Vulnerability, resilience, and resistance. J Neurochem. 2021. 158(6):1394-1411. doi: 10.1111/jnc.15471.
- Wenk GL. The nucleus basalis magnocellularis cholinergic system: one hundred years of progress. Neurobiol Learn Mem. 1997. 67(2):85-95. doi: 10.1006/nlme.1996.3757.
- D'Atri, A. et al. EEG alterations during wake and sleep in mild cognitive impairment and Alzheimer's disease. iScience. 2021. 24(4), 102386. doi:10.1016/j.isci.2021.102386.
- André, C. et al. Associations between REM sleep EEG slowing and brain cholinergic denervation in aging and Mild Cognitive Impairment. Mol Psychiatry. 2026. doi: 10.1038/s41380-026-03635-y.

Acknowledgments

We sincerely thank all the study participants and their families for their time and commitment. We also acknowledge the contributions of our research team and collaborating institutions. This work was supported by the NHMRC SIESTA Synergy Grant.

Further information

- @siesta-synergy.bsky.social
- SIESTA Research
- @siestasynergy
- <http://siesta.sydney.edu.au>
- siesta_admin@sydney.edu.au