Elucidating Circadian and Sleep Phenotypes and Relation to Cognitive Impairment in Alzheimer's Dementia

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Introduction

Although sleep disruption in Alzheimer's disease (AD) pathogenesis has been described, the role of circadian rhythm dysfunction (CRD) is less understood.

Objective

We hypothesize greater CRD and sleep disruption with poorer cognitive function in AD compared to normal cognition.

Methods

Table 1. Subject Groups

MCI-AD	HR (High Risk)	CL (Control)
Mild cognitive impairment (MCI), *APOE*Ɛ4 carriers	Cognitively normal *APOE*Ɛ4 carriers	Cognitively normal *APOE*Ɛ4 non-carriers
N=18	N=19	N=16

- Predictors were evaluated across groups in association with cognition (Mini-Mental State Exam (MMSE)).

Table 2. Predictors

Actigraphy		PSG
Sleep	Circadian	
Sleep fragmentation index (SFI)	Sleep regulatory index (SRI)	Apnea hypopnea index (AHI)*
Sleep efficiency (SE)	Mesor	Recording time with SaO2 < 90%
Total sleep time (TST)	Amplitude	
Wake episodes (WE)	Robustness	
	Intra-daily stability	

- ANOVA or Kruskal-Wallis with Bonferroni adjustment assessed cross-group comparisons. ANCOVA assessed cross-group association of MMSE & sleep/circadian indices.

*AASM scoring criteria (3% desaturation)

Results

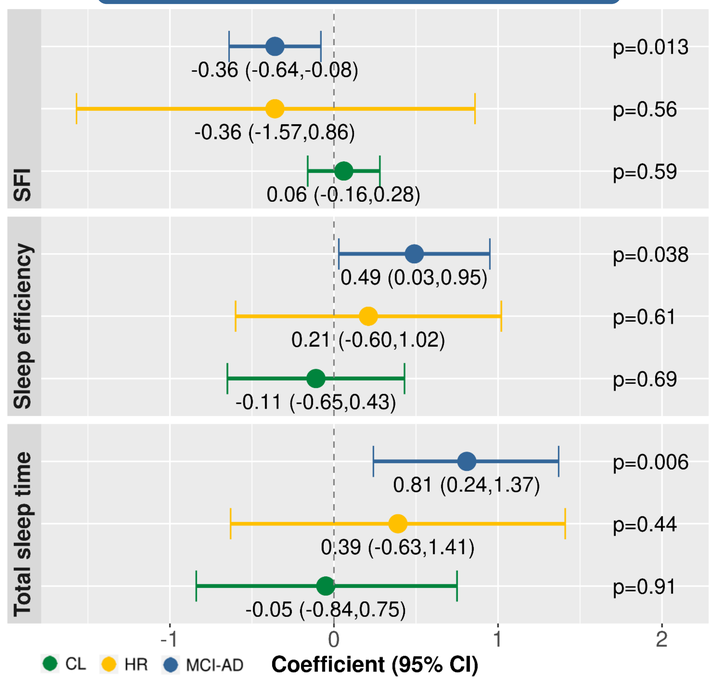

Figure 1. TST, SE, and SFI relationships to MMSE scores

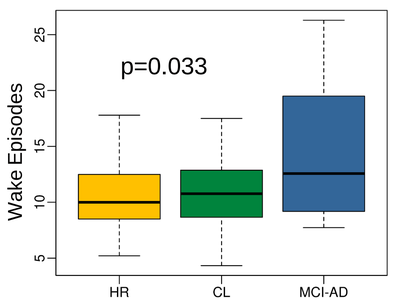

Figure 2. WE among groups

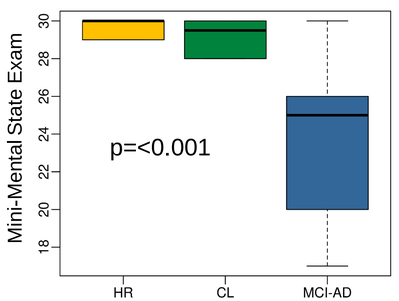

Figure 3. MMSE scores among groups

Table 3. Subject Characteristics

	MCI-AD		HR		CL		p-value
Factor	N	Statistics	N	Statistics	N	Statistics	
Age	18	68.4 ± 6.2	19	71.2 ± 3.7	16	73.7 ± 3.7	***0.008***
Sex, male	18	10 (56%)	19	11 (58%)	16	6 (38%)	0.43
Race	18		19		16		0.065
White		18 (100%)		17 (90%)		12 (75%)	
Black		0 (0%)		2 (10%)		4 (25%)	
Education, yr	18	15.3 ± 2.6	19	17.2 ± 2.6	15	17.3 ± 2.7	0.051
BMI	18	27.5 ± 4.2	15	27.6 ± 3.6	15	27.0 ± 2.1	0.85

- Age differed across groups (p=0.008, **Table 3**)
- Associations in MCI-AD (**Figure 1**):
  - 1 unit increase in SFI assoc. with 0.36 pt. lower MMSE
  - 5% increase in SE assoc. with 0.49 pt. higher MMSE
  - 1 hour increase in TST assoc. with 0.81 pt. higher MMSE
- MCI-AD had more WE than HR and CL (**Figure 2**)
- MMSE scores differed across groups (p=<0.001, **Figure 3**)

Conclusion

- Less total sleep time and more fragmented sleep are associated with poorer MMSE scores in *APOE*Ɛ4 carriers with MCI (MCI-AD).
- Cognitively normal participants at risk of AD (HR group) do not show CRD that is seen in MCI-AD and are more consistent with controls (CL).

Acknowledgements

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