

Relationship Between Subjective Sleep Measures and Regional Cerebellar Volumes Across the Alzheimer’s Disease Continuum

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Background

Sleep disturbances are recognized as a risk factor for Alzheimer’s disease (AD) and may accelerate neurodegenerative changes in the brain. While previous studies have largely focused on cortical and hippocampal regions, the role of the cerebellum remains poorly understood. Therefore, this study aimed to investigate the associations between subjective sleep scales and regional cerebellar volume to clarify the potential impact of sleep disturbances within the AD spectrum.

Methods

Medical records of patients who visited St. Vincent’s Hospital between September 2019 and April 2024 were retrospectively reviewed. Cerebellar gray matter volumes were analyzed using voxel-based morphometry implemented in SPM12. The associations between total scores of the Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI), and Epworth Sleepiness Scale (ESS) and regional cerebellar volumes were examined using partial Spearman’s correlation analyses controlling for age, sex, education, APOE ε4 status, and total intracranial volume. Relationships between each PSQI subcomponent score and regional cerebellar volumes were further assessed using ranked analysis of covariance with the same covariates.

Results

In subjects with Amyloid -β NC normal cognition, good sleepers were associated with smaller gray matter volume in the Vermis Crus I. In contrast, in patients with AD dementia, higher ISI score was correlated with reduced volumes in the Left and Right Crus II, Left and Right VIIb, Left and Right VIIa, Left and Right VIIb, Vermis VIIb, and the posterior lobe.

Conclusion

Sleep disturbance, particularly insomnia, was associated with cerebellar gray matter reduction in AD dementia. These findings suggest that sleep problems may accelerate cerebellar neurodegeneration in the Alzheimer’s spectrum.

Keywords

Sleep initiation and maintenance disorders, cerebellum, Alzheimer disease, cognitive dysfunction

Table 1. Demographic and clinical characteristics of participants according to diagnosis

Characteristics	Aβ- NC (N=49)	Aβ+ NC (N=21)	Aβ+ MCI (N=32)	AD Dementia (N=55)
Male(%)	18(36.7)	8(38.1)	4(12.5)	18 (32.7)
Female(%)	31(63.3)	13(61.9)	28(87.5)	37 (67.3)
Age	71.5±7.65	76.6±7.17	75.6±6.07	75.8±7.29
Education year	8.31±5.48	8.81±4.19	8.50±4.74	8.07±4.86
APOE ε4 allele				
APOE ε4 carrier(%)	10 (20.4)	12 (57.1)	15(46.9)	26(47.3)
APOE ε4 non-carrier(%)	39 (79.6)	9(42.9)	17(53.1)	29(52.7)
Total intracranial volume	1383±154	1381±110	1356±132	1358±115
PSQI Total score	7.55±4.01	7.62±2.50	7.47±2.79	6.98±2.70
Subjective sleep quality				
Very good(%)	4 (8.2)	1(4.8)	5(15.6)	7(12.7)
Fairly good(%)	29 (59.2)	14(66.7)	19(59.4)	39(70.9)
Fairly bad(%)	15 (30.6)	6(28.6)	8(25.0)	9(16.4)
Very bad(%)	1(2.0)	0(0)	0(0)	0(0)
Sleep latency				
Falls asleep within 15min; no difficulty(%)	13(26.5)	5(23.8)	7(21.9)	21(38.2)
16-30min or difficulty <1night /wk(%)	17(34.7)	6(28.6)	12(37.5)	10(18.2)
31-60min or difficulty 1-2 nigh ts/wk(%)	9(18.4)	7(33.3)	7(21.9)	11(20.0)
>60min or difficulty ≥3nights /wk(%)	10(20.4)	3(14.3)	6(18.8)	13(23.6)
Sleep duration				
Sufficient sleep duration(%)	24(49.0)	5(23.8)	9(28.1)	22(40.0)
Mildly shortened sleep (%)	6(12.2)	3(14.3)	6(18.8)	17(30.9)
Moderately short sleep(%)	6(12.2)	8(38.1)	10(31.3)	9(16.4)
Very short sleep duration(%)	13(26.5)	5(23.8)	7(21.9)	7(12.7)
Sleep disturbance				
No sleep disturbance(%)	1(2)	1(4.8)	8(25.0)	7(12.7)
Mild disturbance(%)	44(89.8)	16(76.2)	23(71.9)	48(87.3)
Moderate disturbance(%)	4(8.2)	4(19.0)	2(3.1)	0(0)
Severe disturbance(%)	0(0)	0(0)	0(0)	0(0)
Use of sleep medication				
No use of sleep medication(%)	39(79.6)	19(90.5)	24(75.0)	52(94.5)
Occasional use(%)	0(0)	1(4.8)	1(3.1)	0(0)
Frequent use(%)	1(2.0)	0(0)	2(6.3)	1(1.8)
Regular use(%)	9(18.4)	1(4.8)	5(15.6)	2(3.6)
Daytime dysfunction				
No daytime dysfunction(%)	37(75.5)	15(71.4)	23(71.9%)	42(76.4)
Mild dysfunction(%)	5(10.2)	5(23.8)	5(15.6%)	8(14.5)
Moderate dysfunction(%)	2(4.1)	1(4.8)	3(9.4%)	4(7.3)
Severe dysfunction(%)	5(10.2)	0(0)	1(3.1%)	1(1.8)
Good sleeper(%)	13(26.5)	4(19.0)	4(12.5%)	7(12.7)
Poor sleeper(%)	36(73.5)	17(81.0)	28(87.5)	48(87.3)
ISI Total score	7.67±6.04	8.90±6.90	5.88±5.09	5.37±4.39
ESS Total score	7.02±4.86	5.05±4.52	3.59±3.21	3.52±3.52

NC; normal cognition, Aβ; amyloid- β, MCI; mild neurocognitive impairment, AD; Alzheimer’s disease, PSQI;Pittsburgh sleep quality index, ISI;insomnia severity index, ESS;Epworth sleepiness scale

Figure1. Adjusted Vermis Crus I volume in good versus poor sleepers in Aβ- cognitively normal cognition group

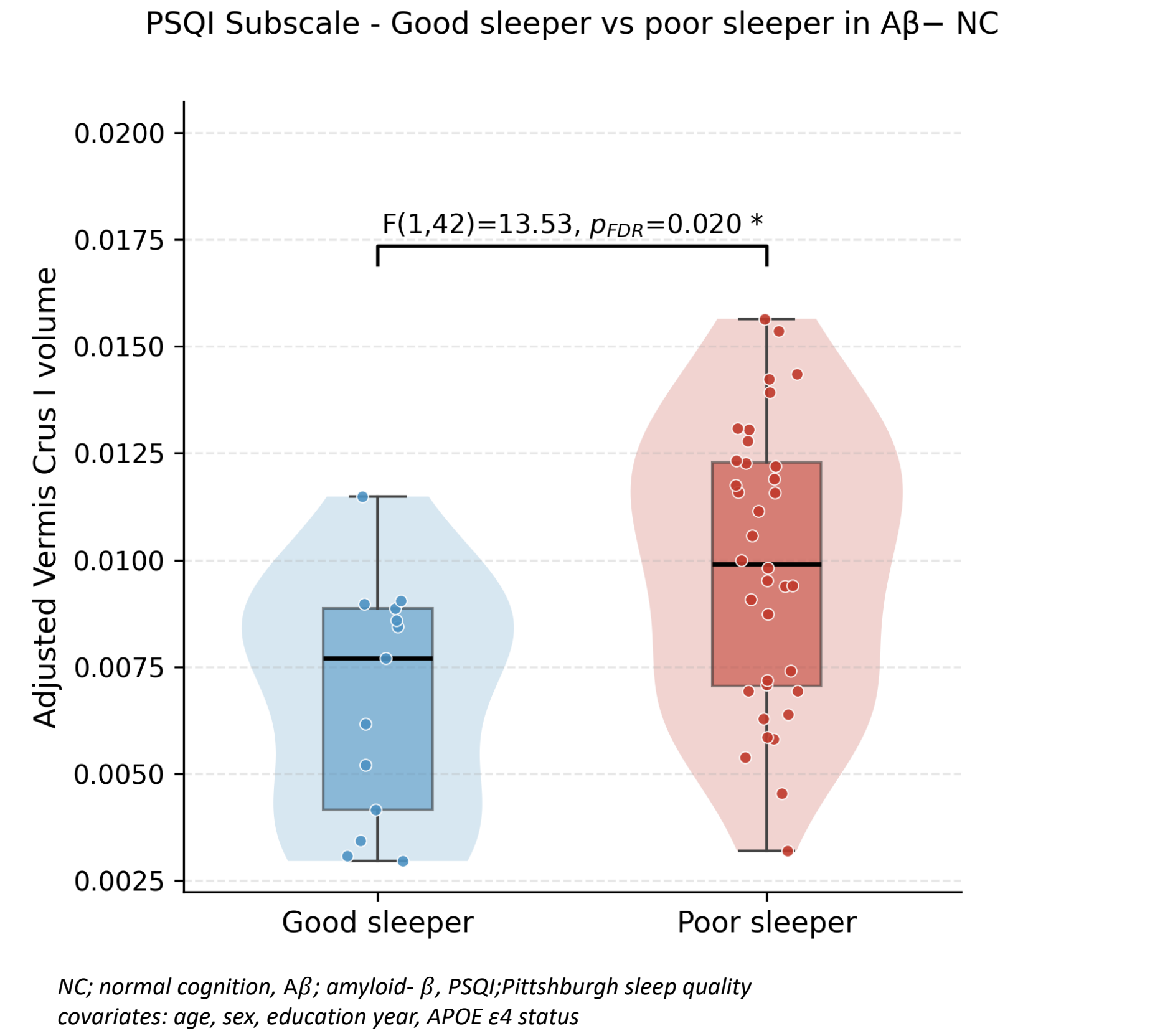


Figure 2. Associations between Insomnia severity index and cerebellar subregional volume loss in Alzheimer’s disease dementia

