Supplementary Material

Table S1. Local effect size of midline estimation statistic of rhythm (MESOR) for dependent variables and included covariates in multiple linear regression analysis.

Table S2. Local effect size of least active 5-h (L5) onset time for dependent variables and included covariates in multiple linear regression analysis.

Table S3. Severity of white matter hyperintensities (WMHs) in study participants.

Fig S1. Flow diagram of study participants.

Fig S2. Distributions of rest-activity pattern variables.

Table S1. Local effect size of MESOR for dependent variables and included covariates in multiple linear regression analysis[*]

| Dependent variables | Independent variable: MESOR | | | | | |
| | All Participants (n=100) | | Amyloid Negative (n=54) | | Amyloid Positive (n=46) | |
	Covariates included[a]	Cohen's f^2 for MESOR[†, ‡]	Covariates included	Cohen's f^2 for MESOR	Covariates included	Cohen's f^2 for MESOR
Neuroimaging biomarkers						
Cortical amyloid burden, SUVR	Age, education, ACEi use, and APOE ε4 allele carrier status	< 0·01	No covariates included	NA	ACEi use	< 0·01
Medial temporal lobe GM volume	Age, sex, diabetes, ACEi use, and APOE ε4 allele carrier status	0·02	Age, sex, diabetes	0·01	Age, ACEi use, sleep medication use, and APOE ε4 allele carrier status	0·01
Cognitive function						
Language function	Age, sex, education, living alone, ACEi use, and APOE ε2 allele carrier status	0·02	Education, and APOE ε2 allele carrier status	0·03	Education, living alone, ACEi use, and APOE ε4 allele carrier status	0·01
Visuospatial function	Education and APOE ε2 allele carrier status	< 0·01	Education, diabetes, and number of weekend days	0·06	Education and ACEi use	0·01
Memory function	Education, ACEi use, APOE ε2 allele carrier and ε4 allele carrier status	< 0·01	Education and APOE ε2 allele carrier status	0·01	Education and ACEi use	< 0·01
Frontal/executive function	Education, living alone, ACEi use, antipsychotics use, and APOE ε2 allele carrier status	0·08	Education, living alone, antipsychotics use, and APOE ε2 allele carrier status	0·17	Sex, education, living alone, and APOE ε4 allele carrier status	0·03

ACEi, acetylcholine esterase inhibitor; APOE, apolipoprotein E; GM, grey matter; MESOR, midline estimation statistic of rhythm; SUVR, standardized uptake value ratio

* We adjusted for age, sex, education, living alone, diabetes, hypertension, depressive symptoms, acetylcholine esterase inhibitor use, antidepressant use, antipsychotics use, benzodiazepine use, sleep medication use, number of weekend days, and apolipoprotein -ε allele carrier status using a forward stepwise method. MESOR was directly entered into the regression model.
† We measured local effect size of MESOR using a variation of Cohen's f^2 according to the following equation: local effect size = $(R^2_{MC} - R^2_C)/(1 - R^2_{MC})$, where R^2_{MC} = proportion of variance accounted for by MESOR and covariates together, R^2_C = proportion of variance accounted for by covariates.
‡ According to Cohen's guidelines, $f^2 \geq 0.02$, $f^2 \geq 0.15$, and $f^2 \geq 0.35$ represent small, medium, and large effect sizes, respectively.

Table S2. Local effect size of L5 onset time for dependent variables and included covariates in multiple linear regression analysis[*]

| Dependent variables | Independent variable: L5 onset time | | | | | |
| | All participants (n=100) | | Amyloid-negative (n=54) | | Amyloid-positive (n=46) | |
	Covariates included[a]	Cohen's f^2 for L5 onset time[†, ‡]	Covariates included	Cohen's f^2 for L5 onset time	Covariates included	Cohen's f^2 for L5 onset time
Neuroimaging biomarkers						
Cortical amyloid burden, SUVR	Age, education, ACEi use, and APOE ε4 allele carrier status	0·02	No covariates included	NA	ACEi use	< 0·01
Medial temporal lobe GM volume	Age, sex, ACEi use, and APOE ε4 allele carrier status	0·04	Age, sex, and diabetes	0·28	ACEi use	< 0·01
Cognitive function						
Language function	Age, sex, education, ACEi use, and APOE ε2 allele carrier status	0·03	Education, and APOE ε2 allele carrier status	0·06	Age, education, and ACEi use	0·01
Visuospatial function	Age, education, and ACEi use	0·02	Education, diabetes, and number of weekend days	0·03	Education and ACEi use	0·06
Memory function	Education, ACEi use, and APOE ε2 allele and ε4 allele carrier status	0·02	Education, and APOE ε2 allele carrier status	0·19	Education and ACEi use	< 0·01
Frontal/executive function	Age, education, ACEi use, antipsychotics use, and APOE ε2 allele carrier status	0·07	APOE ε2 allele carrier status	0·09	Sex, education, living alone, and APOE ε4 allele carrier status	0·15

ACEi, acetylcholine esterase inhibitor; APOE, apolipoprotein E; GM, grey matter; L5 onset time, least active 5-h onset time; SUVR, standardized uptake value ratio

* We adjusted for age, sex, education, living alone, diabetes, hypertension, depressive symptom, acetylcholine esterase inhibitor use, antidepressant use, antipsychotics use, benzodiazepine use, sleep medication use, number of weekend days, and apolipoprotein -ε allele carrier status using a forward stepwise method. L5 onset time was directly entered into the regression model.

[†] We measured the local effect size of L5 onset time using a variation of Cohen's f^2 according to the following equation: local effect size = $(R^2_{LC} - R^2_{C})/(1 - R^2_{LC})$, where R^2_{LC} = proportion of variance accounted for by L5 onset time and covariates together, R^2_{C} = proportion of variance accounted for by covariates.
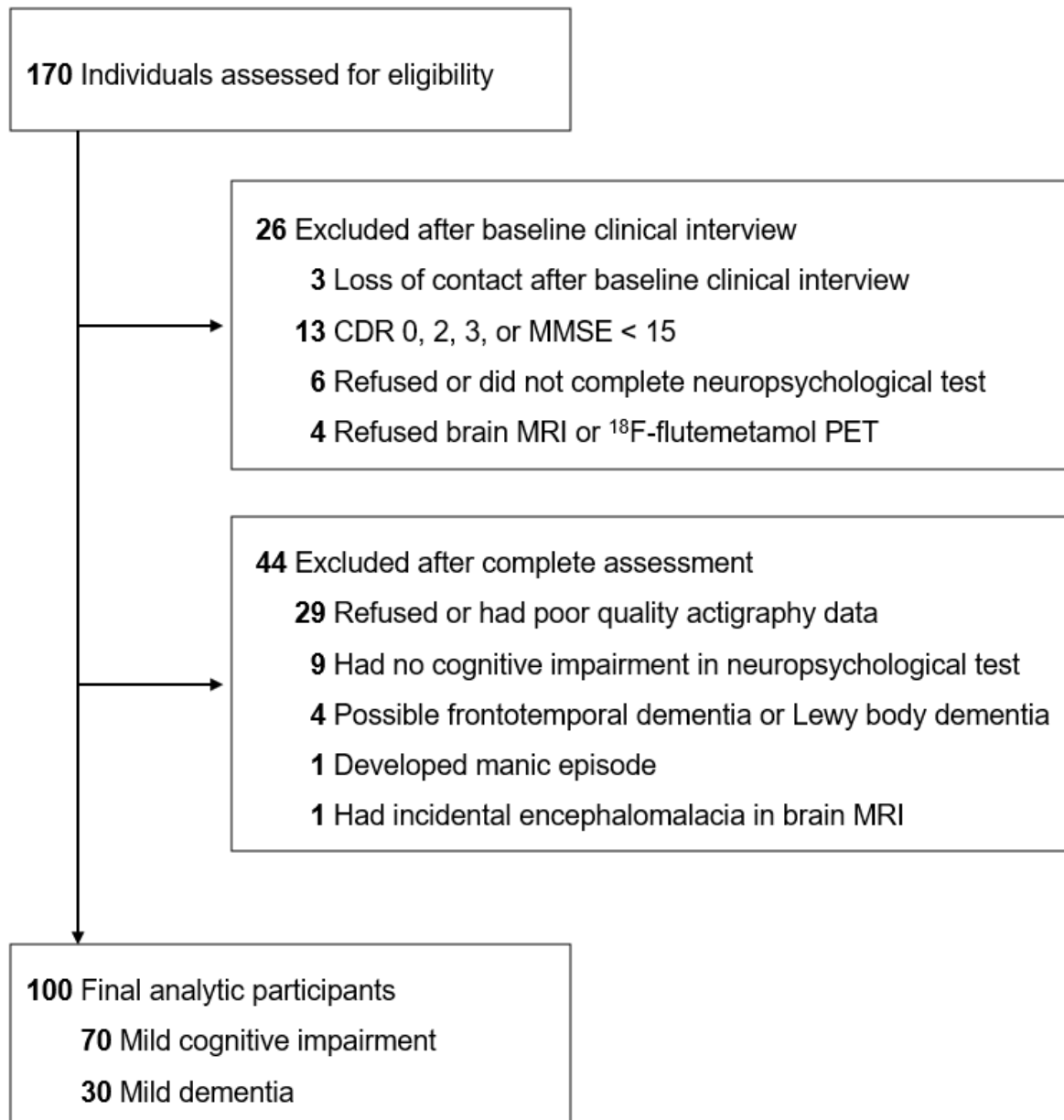
[‡] According to Cohen's guidelines, $f^2 \geq 0.02$, $f^2 \geq 0.15$, and $f^2 \geq 0.35$ represent small, medium, and large effect sizes, respectively.

Table S3. Severity of white matter hyperintensities (WMHs) in study participants.

	Amyloid-Negative		Amyloid-Positive	
	N	%	N	%
WMHs severity				
- Mild severity	35	64·8	30	65·2
- Moderate severity	14	25·9	11	23·9
- Severe severity	5	9·3	5	10·9

P-value for chi-square test = 0.949

Fig S1. Flow diagram of study participants.

170 Individuals assessed for eligibility

26 Excluded after baseline clinical interview
 3 Loss of contact after baseline clinical interview
 13 CDR 0, 2, 3, or MMSE < 15
 6 Refused or did not complete neuropsychological test
 4 Refused brain MRI or ^{18}F-flutemetamol PET

44 Excluded after complete assessment
 29 Refused or had poor quality actigraphy data
 9 Had no cognitive impairment in neuropsychological test
 4 Possible frontotemporal dementia or Lewy body dementia
 1 Developed manic episode
 1 Had incidental encephalomalacia in brain MRI

100 Final analytic participants
 70 Mild cognitive impairment
 30 Mild dementia

CDR, Clinical Dementia Rating; MMSE, Mini-Mental Status Examination; MRI, magnetic resonance imaging; PET, positron emission tomography

Fig S2. Distributions of rest-activity pattern variables.
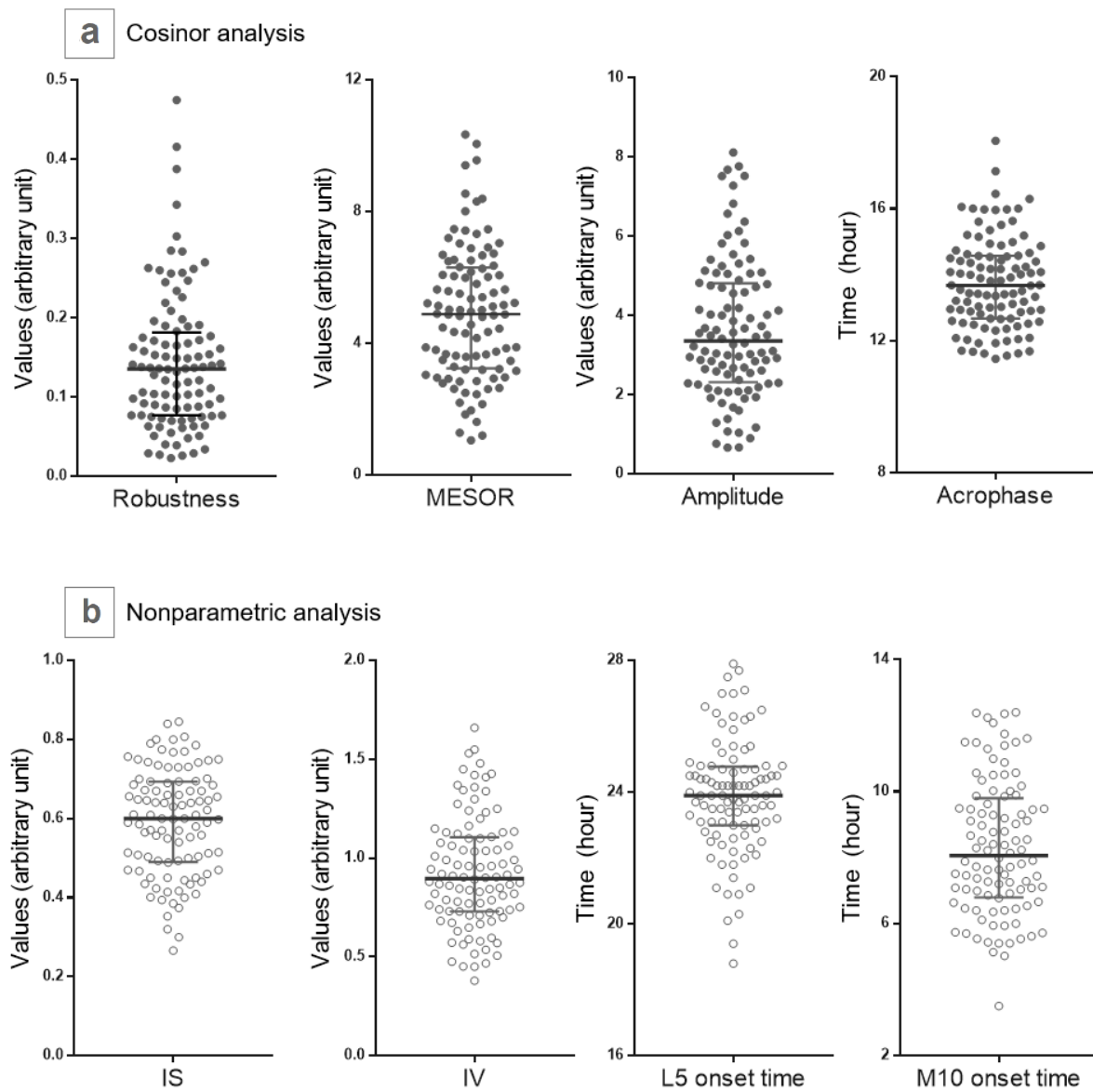
Rest-activity pattern variables are expressed as arbitrary units, except for the three phase-associated variables (acrophase, L5 onset time, and M10 onset time). Circles indicate patients. Bars in the middle indicate medians, while error bars indicate Interquartile range. IS, inter-daily stability; IV, intra-daily variability; L5 onset time, least active 5-h onset time; M10 onset time, most active 10-h onset time; MESOR, midline estimation statistic of rhythm