

Supplemental Figures and Tables

	Model	AIC	BIC	RMSE	Sigma	R ² cond.	R ² marg.	ICC
(a) Main Model	(1) Composite Model	5148.8	5246.7	0.633	0.670	0.377	0.223	0.197
(b) Single Index	(2) ChPV Only	1573.8	1611.8	0.226	0.311	0.952	0.067	0.949
	(3) PVSV Only	550.8	588.6	0.113	0.156	0.972	0.177	0.966
	(4) FWI Only	468.4	498.9	0.121	0.172	0.995	0.046	0.995
	(5) ALPS Only	496.4	526.6	0.183	0.253	0.983	0.009	0.983
(c) Post Hoc	(6) Composite Excl. ChPV	2937.8	3012	0.517	0.564	0.459	0.249	0.280
	(7) Composite Incl. BPF	5232.6	5433.2	0.639	0.676	0.368	0.219	0.192

Table S1: Mixed effect models and metrics. Model performance is shown for **(a)** the main composite index model, **(b)** single-index models, and **(c)** the post hoc models, including an enhanced composite index model excluding the ChPV (6) and a composite index model including the BPF interaction term (7). Optimal values across performance measures are highlighted in yellow. Values highlighted in grey were fit on different (sub-)datasets and can thus only be compared to historical controls. While composite index models generally performed worse across most evaluation metrics, they achieved higher marginal R², indicating that the inclusion of multiple indices improved fixed-effect explanatory power despite reduced overall model fit.

AIC = Akaike information criterion, ALPS = along the perivascular space, BIC = Bayesian information criterion, BPF = brain parenchymal fraction, ChPV = choroid plexus volume, cond. = conditional, FWI = free water index, ICC = intraclass correlation coefficient, marg. = marginal, PVSV = perivascular space volume, RMSE = root mean squared error.

Dataset	Scanner	Sequence	TR (ms)	TE (ms)	TI (ms)	Flip Angle (°)	Publication
Bruxelles	Siemens Prisma	MPRAGE	1900	2.19	900	9	Stee et al. ⁵⁹
Christchurch	GE Signa HDx	BRAVO	6.5	2.80	400	n.r.	Poudel et al. ⁵⁷
Cologne (1)	Siemens Biograph mMR	MPRAGE	2250	3.03	900	9	Hennecke et al. ⁵⁵
Cologne (2)	Siemens Biograph mMR	MPRAGE	2250	3.03	900	9	Lin et al. ⁵⁶
Juelich	Siemens TrioTim	MPRAGE	2000	3.03	900	9	Elmenhorst et al. ⁶⁵
Montreal	GE Discovery MR750	BRAVO	8.2	3.18	450	12	Cross et al. ⁶⁰
Oslo	Siemens Prisma	MEMPRAGE	2530	1.69	1100	7	Voldsbekk et al. ⁶¹
		<i>*first echo only</i>					
Singapore	Siemens TrioTim	MPRAGE	2000	2.98	900	9	Yeo et al. ⁶²
Stockholm	GE Discovery MR750	BRAVO	6.4	2.81	450	11	Nilsson et al. ⁵⁸
Trondheim	Siemens Skyra	MPRAGE	2300	2.92	900	9	Smevik et al. ⁶³
Zurich	GE Signa PET/MR	BRAVO	8.4	3.22	600	8	Weigend et al. ⁶⁴

Table S2: Acquisition parameters for T1-weighted MRI scans across ENIGMA-Sleep cohorts. All T1-weighted anatomical images were acquired on 3T MRI scanners with 1 mm³ isotropic voxel resolution.

MRI = magnetic resonance imaging, n.r. = not reported, T = tesla, TE = echo time, TI = inversion time, TR = repetition time, PET = positron emission tomography.

Dataset	Scanner	Sequence	Resolution (mm ³)	TR (ms)	TE (ms)	b-values	PED	Publication
Bruxelles	Siemens Prisma	Multiband EPI <i>*acc.factor 2</i>	2 x 2 x 2	4070	70	0, 650, 1000, 2000	AP/PA	Stee et al. ⁵⁹
Juelich	Siemens TrioTim	DTI EPI	2.4 x 2.4 x 2.4	8300	111	0, 700, 1000, 2850	AP	Elmenhorst et al. ⁶⁵
Oslo	Siemens Prisma	DTI EPI	2 x 2 x 2	2450	85	0, 500, 1000, 2000	AP/PA	Voldsbekk et al. ⁶¹
Trondheim	Siemens Skyra	DTI EPI	2 x 2 x 2	4000	116	0, 1000	AP	Smevik et al. ⁶³

Table S3: Acquisition parameters for diffusion MRI scans across ENIGMA-Sleep cohorts. All diffusion images were acquired on 3T MRI scanners. B-values are reported as nominal diffusion shells.

acc. = acceleration, *AP* = anterior-to-posterior, *DTI* = diffusion tensor imaging, *EPI* = echo-planar imaging, *MRI* = magnetic resonance imaging, *TE* = echo time, *TR* = repetition time, *PA* = posterior-to-anterior, *PED* = phase encoding direction.

Dataset	Day	Protocol	Publication
Bruxelles	-3	Adaptation night (6–8h TIB) with hd-EEG	Stee et al. ⁵⁹
	0	NS (at home) → MRI acq. pre- and post-SRTT (16:30–20:30)	
	1	SD (22h) or NS (6–8h TIB) with hd-EEG → MRI acq. and SRTT retest (8:30)	
	4	NS (at home) → MRI acq. pre- and post-SRTT (16:30–20:00) <i>*control subjects were not included/available for the present study</i>	
Christchurch	-7 to -1	NS (at home) with actigraph and diary	Poudel et al. ⁵⁷
	0	SR (4h TIB) or NS (at home) → MRI acq. with VTT (13:00–14:30)	
	1	NS (at home) or SR (4h TIB) → MRI acq. with VTT (13:00–14:30)	
Cologne (1)	-1	NBT (21:00) → adaptation night (8h TIB) with PSG → NBT (9:00–11:00 +1)	Hennecke et al. ⁵⁵
	0	NBT (21:00) → NS (8h TIB) with PSG → NBT (9:00–11:00 +1)	
	1	NBT (21:00) → NS (8h TIB) with PSG → MRI acq. and NBT (9:00–11:00 +1)	
	2 to 5	NBT (21:00) → SR (5h TIB) or NS (8h TIB) with PSG → NBT (9:00–11:00 +1)	
	6	NBT (21:00) → SR (5h TIB) or NS (8h TIB) with PSG → MRI acq. and NBT (9:00–11:00 +1)	
	7	NBT (21:00) → NS (8h TIB) with PSG → MRI acq. and NBT (9:00–11:00 +1)	
	8	NBT (21:00) → SD (24h) → MRI acq. and NBT (9:00–11:00 +1)	
	9	NS (8h TIB) with PSG → MRI acq. and NBT (9:00 +1) <i>*SR sessions were not included/available for the present study</i>	

Cologne (2)	-1	Adaptation night (8h TIB)	Lin et al. ⁵⁶
	0	NS (8h TIB) → SALS (16:00, 23:00)	
	1	NS (8h TIB) → MRI acq. (16:00) and SALS (16:00, 23:00)	
	2 to 5	SR (5h TIB) → 200 mg (8:00) and 100 mg (13:00) caffeine or decaf and SALS (23:00)	
	6	SR (5h TIB) → MRI acq. (16:00) , 200 mg (8:00) caffeine or decaf, and SALS (16:00, 23:00)	
	7	NS (8h TIB) → MRI acq. (16:00) and SALS (16:00)	
		<i>*caffeinated subjects were excluded from the present study</i>	
Juelich	-8 to -2	NS (at home, 9h TIB)	Elmenhorst et al. ⁶⁵
	-1	Adaptation night (at home, 9h TIB) with EEG	
	0	NS (at home, 9h TIB) with EEG → MRI acq., PVT, and KSS (7:00–11:00) → PET (11:00)	
	1	SD (at home, 24h) or NS (at home, 9h TIB) with EEG → MRI acq., PVT, and KSS (7:00–11:00) → PET (11:00) → SD group 2h nap with EEG	
Montreal	-1	Adaptation night (8h TIB)	Cross et al. ⁶⁰
	0	SD (24h) or NS (8h TIB) → MRI acq., ANT, NBT, and MCT → SD group 60 min. nap → retest	
	1	NS (8h TIB) or SD (24h TIB) → MRI acq., ANT, NBT, and MCT → SD group 60 min. nap → retest	
Oslo	-7 to -1	NS (at home) with actigraph and diary	Voldsbekk et al. ⁶¹
	0	NS (at home) → MRI acq. (9:00, 20:00), PVT and KSS (9:00–23:00)	
	1	NS (8h TIB) or SD with PVT and KSS (23:00–16:00) → MRI acq. (9:00, 20:00)	

Singapore	-1	NS (at home) with actigraph	Yeo et al. ⁶²
	0	SD (24h) with KSS and PVT (19:00–5:00) or NS (9h TIB) → MRI acq. and PVT (6:00–8:00)	
	7	NS (9h TIB) or SD (24h) with KSS and PVT (19:00–5:00) → MRI acq. and PVT (6:00–8:00)	
Stockholm	0	SR (at home, 3h TIB) or NS (at home) with PSG → MRI acq., KSS, and PVT (18:00–23:00)	Nilsson et al. ⁵⁸
	31	NS (at home) or SR (at home, 3h TIB) with PSG → MRI acq., KSS, and PVT (18:00–23:00) <i>*scanning sessions at least a month apart</i>	
Trondheim	-8	NS (at home) → CPT-3, PSQI, ISI, ESS, MEQ, CFS, and sleep duration weekends vs. weekdays	Smevik et al. ⁶³
	-7 to -1	NS (at home) with actigraph	
	0	NS (at home) with actigraph → MRI acq. with KSS and Not-X-CPT (8:00–15:00)	
	1-3	NS (at home) with actigraph	
	4-6	SR (at home, NS -3h) or NS (at home) with actigraph	
	7	SR (at home, NS -3h) or NS (at home) with actigraph → MRI acq. with KSS (8:00–15:00)	
	8 to 10	NS (at home) with actigraph	
	11 to 13	SR (at home, NS -3h) or NS (at home) with actigraph	
	14	SR (at home, NS -3h) or NS (at home) with actigraph → MRI acq. with KSS (8:00–15:00) <i>*SR protocol (days 1-14) not yet published</i>	

Zurich	-1	Adaptation night (8h TIB)	Weigend et al. ⁶⁴
	0	NS (8h TIB) → MRI acq., (PET acq.) and blood draw (~16:23)	
	1	SD (40h) with PVT, KSS, TSS, and VAS → MRI acq., (PET acq.) and blood draw (~16:23)	
	2	NS (10h TIB) → MRI acq., (PET acq.) and blood draw (~16:23)	

Table S4: Sleep reduction protocols across ENIGMA-Sleep cohorts. Data used in the present study as NS baseline highlighted in green. Data used as SR or SD follow-up highlighted in purple. Note that four studies (Christchurch, Montreal, Singapore, Stockholm) employed a cross-over design and three studies (Bruxelles, Oslo, Trondheim) included a randomly assigned control group.

acq. = acquisition, *ANT* = attention network task, *CFS* = chronic fatigue scale, *CPT-3* = continuous performance test 3rd edition, *ESS* = Epworth sleepiness scale, *hd-EEG* = high-density electroencephalography, *h* = hour, *ISI* = insomnia severity index, *KSS* = Karolinska sleepiness scale, *MCT* = motor control task, *MEQ* = Morningness-Eveningness questionnaire, *MRI* = magnetic resonance imaging, *NBT* = n-back task, *NS* = normal sleep, *PET* = positron emission tomography, *PSG* = polysomnography, *PSQI* = Pittsburgh sleep quality index, *PVT* = psychomotor vigilance task, *SALS* = saliva samples, *SD* = sleep deprivation, *SR* = sleep restriction, *SRTT* = serial reaction time task, *TIB* = time in bed, *TSS* = tiredness symptoms scale, *VAS* = visual analogue scale, *VTT* = visuomotor tracking task.

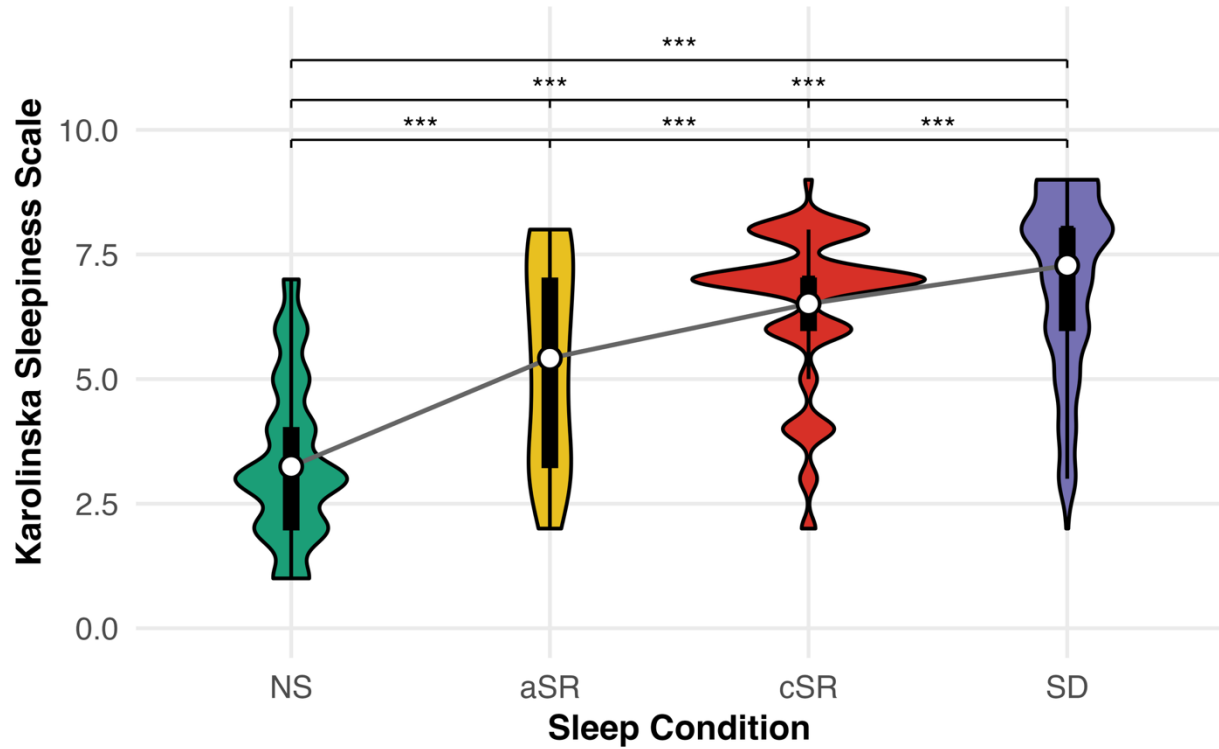


Figure S1: Self-reported sleepiness across sleep conditions. Karolinska Sleepiness Scale scores following normal sleep, acute (1 night) sleep restriction, chronic (3-5 nights) sleep restriction, and total sleep deprivation. Violin and box plots show raw distributions and medians. Group differences across sleep conditions were assessed using a cumulative linked mixed model with estimated marginal means. Self-reported sleepiness increased significantly across successive sleep conditions. Statistical significance was defined as $p < 0.05$ following FDR correction.

aSR = acute sleep restriction, cSR = chronic sleep restriction, FDR = false discovery rate, KSS = Karolinska sleepiness scale, NS = normal sleep, SD = sleep deprivation.

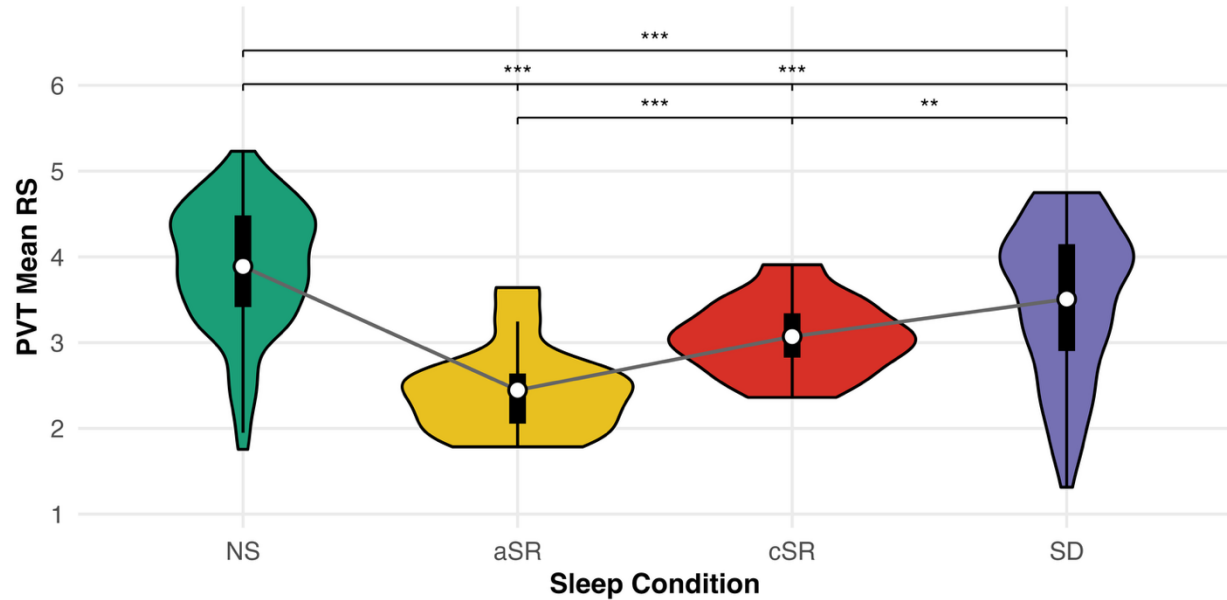


Figure S2: Psychomotor vigilance across sleep conditions. Psychomotor Vigilance Test mean reaction speed (1/s) following normal sleep, acute (1 night) sleep restriction, chronic (3-5 nights) sleep restriction, and total sleep deprivation. Violin and box plots show raw distributions and means. Group differences across sleep conditions were assessed using a linear mixed effects model with estimated marginal means. Compared with normal sleep, reaction speed was reduced following chronic sleep restriction and sleep deprivation. While the raw mean of acute sleep restriction was significantly different than the raw mean of normal sleep, its effect in the linear mixed effects model was only marginally significant ($p = 0.06$). Statistical significance was defined as $p < 0.05$ following FDR correction.

aSR = acute sleep restriction, cSR = chronic sleep restriction, FDR = false discovery rate, NS = normal sleep, PVT = psychomotor vigilance task, RS = reaction speed, s = seconds, SD = sleep deprivation.

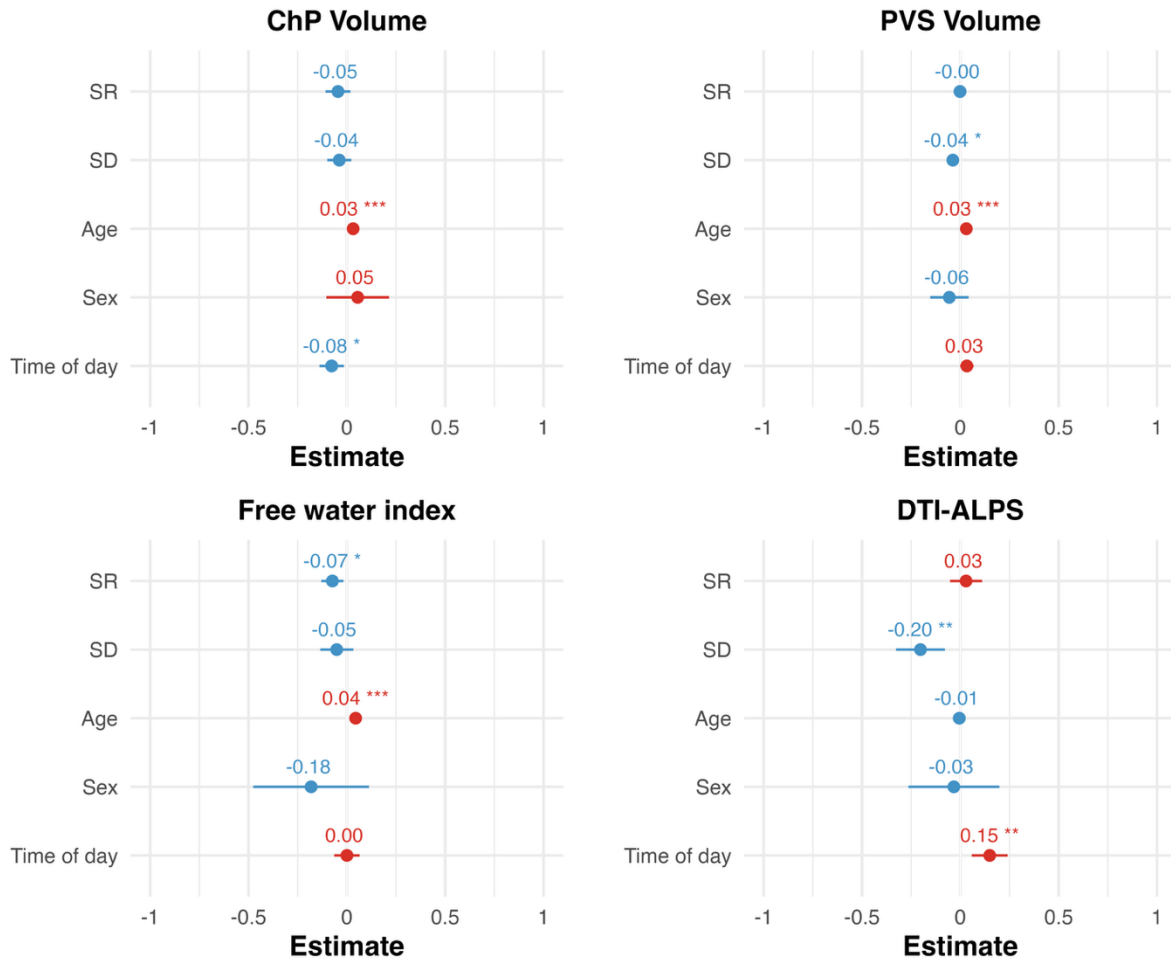


Figure S3: Single-index model estimates. Results from four separate linear mixed-effects models trained on ChPV, PVSV, FWI, and ALPS indices. Significant effects largely replicate those observed in the composite model, including age-related effects in ChPV, PVSV, and FWI, as well as reductions in PVS and ALPS following sleep deprivation and a reduction in FWI following sleep restriction. Statistical significance was defined as $p < 0.05$ following FDR correction.

ALPS = along the perivascular space, *ChPV* = choroid plexus volume, *DTI* = diffusion tensor imaging, *FDR* = false discovery rate, *FWI* = free water index, *PVSV* = perivascular space volume, *SD* = sleep deprivation, *SR* = sleep restriction.

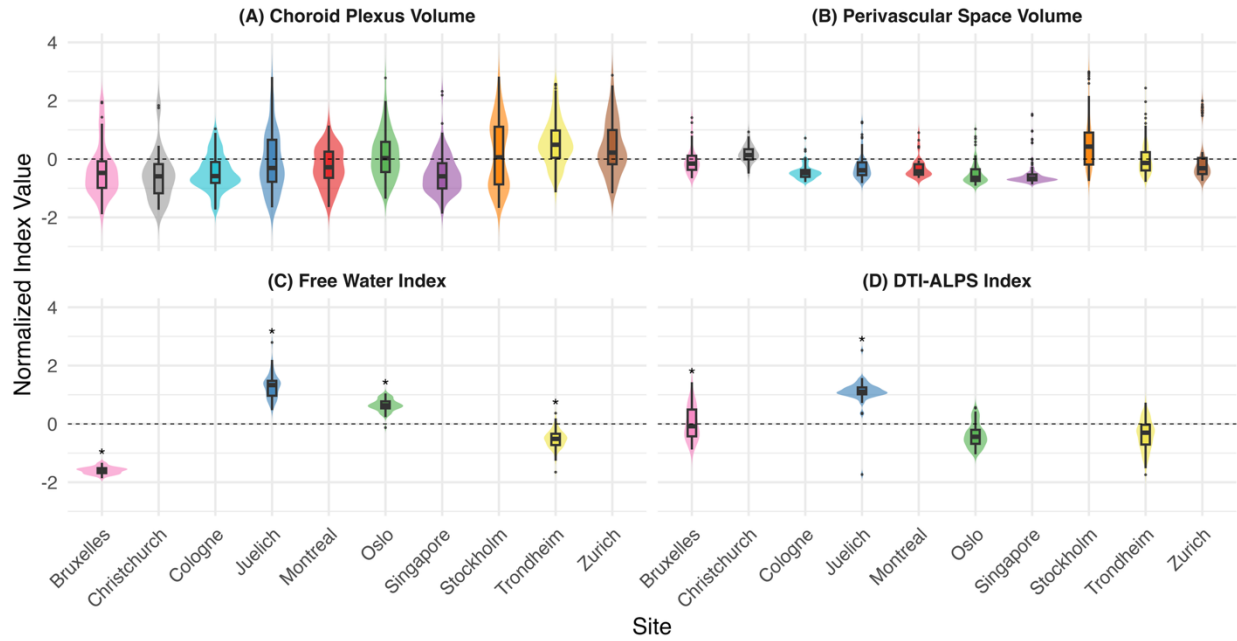


Figure S4: Site-based variability across MRI indices. Distributions of normalized MRI index values by site are shown using violin and box plots. Site-related variability was assessed using linear regression comparing estimated marginal means from each site against all other sites. No significant site effects were observed for ChPV or PVSV. ALPS showed moderate site-related variability, with two sites reaching significance. In comparison, FWI showed pronounced site-related variability, with all sites reaching significance. Statistical significance was defined as $p < 0.05$ following FDR correction.

ALPS = along the perivascular space, ChPV = choroid plexus volume, DTI = diffusion tensor imaging, FDR = false discovery rate, FWI = free water index, PVSV = perivascular space volume

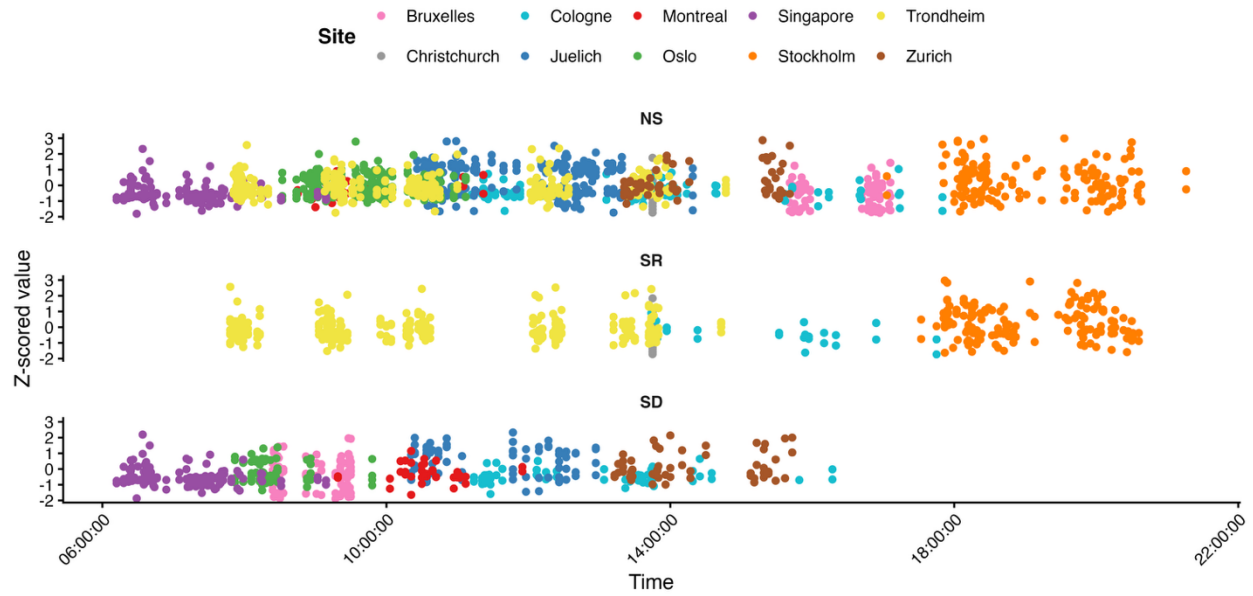


Figure S5: Time of day of MRI acquisition by site. Scatter plot showing acquisition times across sleep conditions, with dot colours indicating sites. The majority of data were acquired between 06:00 and 15:00.

ALPS = along the perivascular space, *ChPV* = choroid plexus volume, *DTI* = diffusion tensor imaging, *FWI* = free water index, *NS* = normal sleep, *PVSV* = perivascular space volume, *SD* = sleep deprivation, *SR* = sleep restriction.

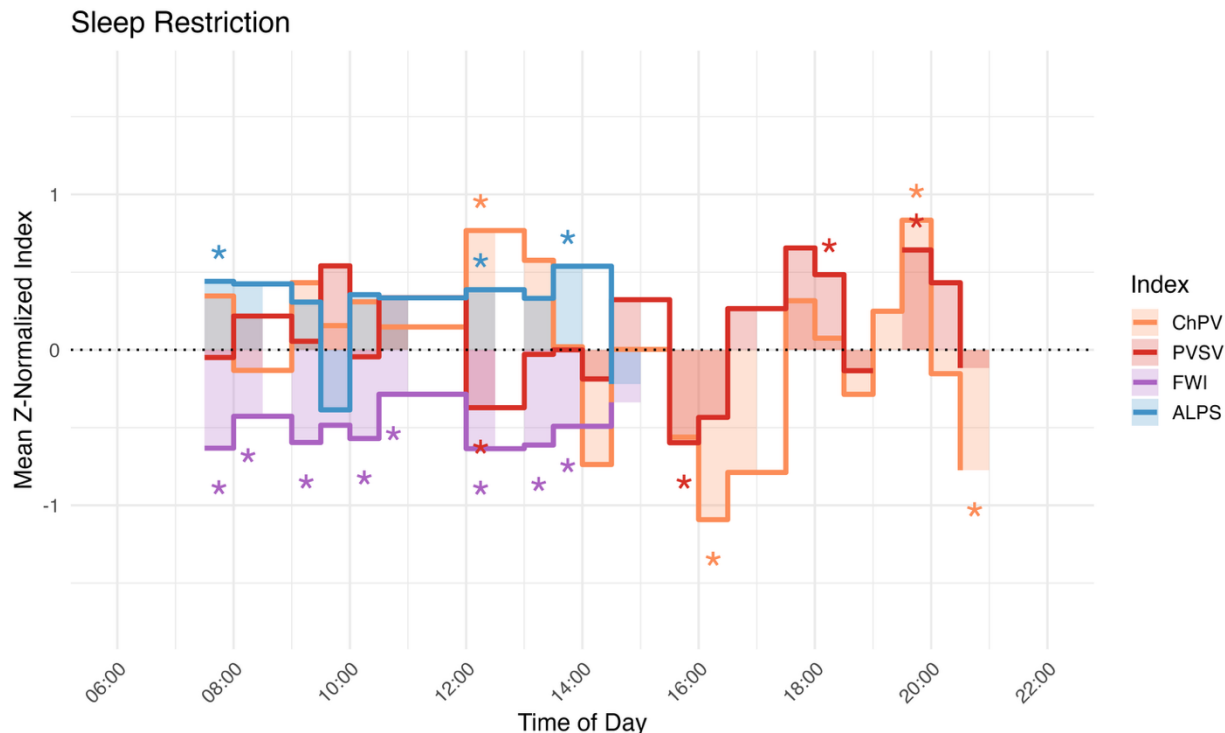


Figure S6: Diurnal changes of MRI indices following sleep restriction. Normalized MRI index values were aggregated in 30-minute time bins. Statistical significance at each time bin was assessed using one-sample t-tests against zero, with bins containing fewer than two data points excluded. Similar to findings in NS and SD, PVSV were low for early and high for late acquisition times. ALPS also appeared anticorrelated with FWI, though there was no change between early and late morning. The ChPV fluctuated significantly across various acquisition periods. Statistical significance was defined as $p < 0.05$ following FDR correction.

ALPS = along the perivascular space, *ChP(V)* = choroid plexus (volume), *DTI* = diffusion tensor imaging, *FDR* = false discovery rate, *FWI* = free water index, *PVS(V)* = perivascular space (volume).

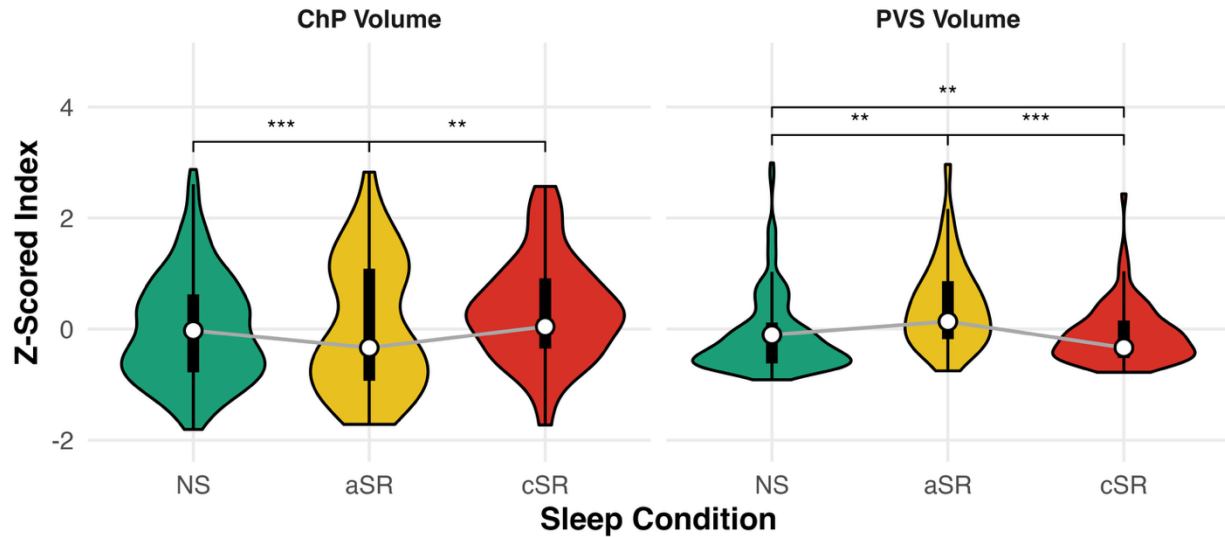


Figure S7: MRI index alterations between acute and chronic sleep restriction assessed using a linear mixed-effects model with estimated marginal means. ALPS and FWI were excluded due to insufficient contrasts. ChPV decreased following acute sleep restriction but remained unchanged following chronic sleep restriction. PVSV increased in both acute and chronic conditions, with a more pronounced increase after acute restriction. Statistical significance was defined as $p < 0.05$ following FDR correction.

ALPS = along the perivascular space, aSR = acute sleep restriction, ChPV = choroid plexus volume, cSR = chronic sleep restriction, DTI = diffusion tensor imaging, FDR = false discovery rate, FWI = free water index, NS = normal sleep, PVSV = perivascular space volume.