Sleep Disturbances are Associated with Brain Structural Covariance Networks in Preadolescence

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Beyond isolated brain regions:

Are sleep disturbances reflected in how the developing brain is organized?

Background

- Sleep disturbances (SD) affect 30–40% of children and are associated with adverse developmental outcomes [1].
- Preadolescence is marked by reorganization of brain morphology, reflected in coordinated structural variation across distributed brain systems [2].
- Existing group-level evidence has linked SD to regional brain structural alterations; however, little is known about how SD relate to individual-specific deviations in brain structural covariance organization and their developmental course.

Research Aim

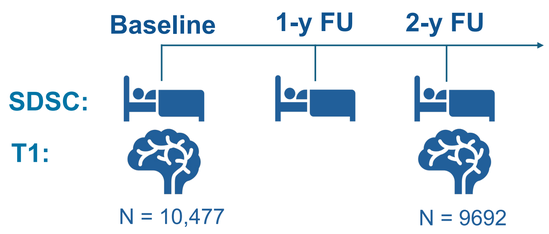
1. Characterize individual-specific alterations in brain structural covariance organization in children with SD.
2. Determine whether these individual-specific alterations form a shared pattern across children with SD.
3. Examine the developmental course of the shared structural covariance pattern according to sleep-disturbance status.

Sample Overview

ABCD — Adolescent Brain Cognitive Development®

Subjects	10,447
Age	9–10 years old at baseline
Follow-up	2-year
Sleep	Sleep Disturbance Scale for Children (SDSC)
Imaging	T1-weighted MRI
Covariates	Age, Sex, BMI, Puberty Stage, Site, Total Intracranial Volume (TIV)

Data Preparation



Inclusion criteria: at least one available T1-weighted MRI

FU: follow-up

Sleep Phenotyping

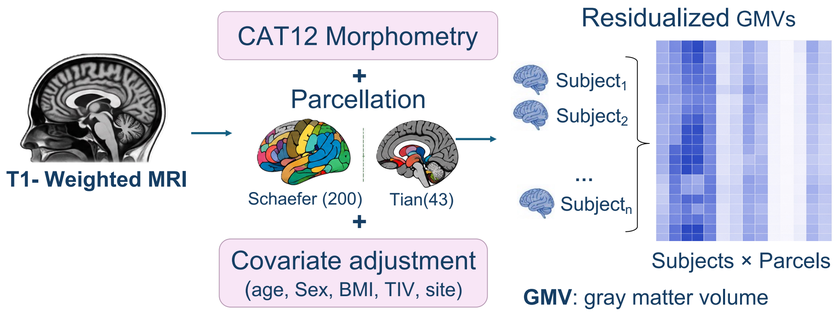
Clinical cut-off: SDSC Total Score ≥ 39

Stable Good sleepers (Never SD) — SDSC Total Score < 39 at all available assessments — Baseline: n = 4420; 2-y FU: n = 3995

With SD history — SDSC Total Score ≥ 39 at least at one time point — Baseline: n = 6057; 2-y FU: n = 5697

Baseline		2-y FU	
Current SD n = 3182	**Current non-SD** n = 2875	**Current SD** n = 2850	**Current non-SD** n = 2847

MRI Processing

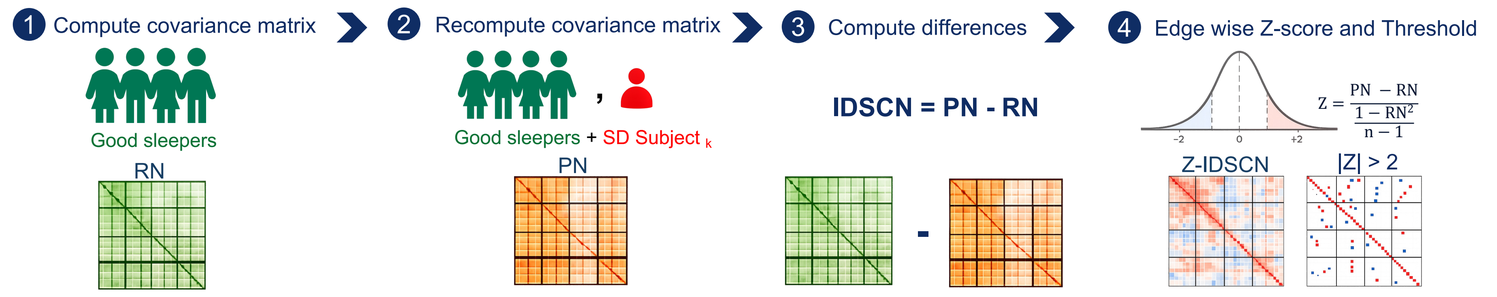


GMV: gray matter volume

Aim 1

Individual Differences in Structural Covariance Organization

Approach



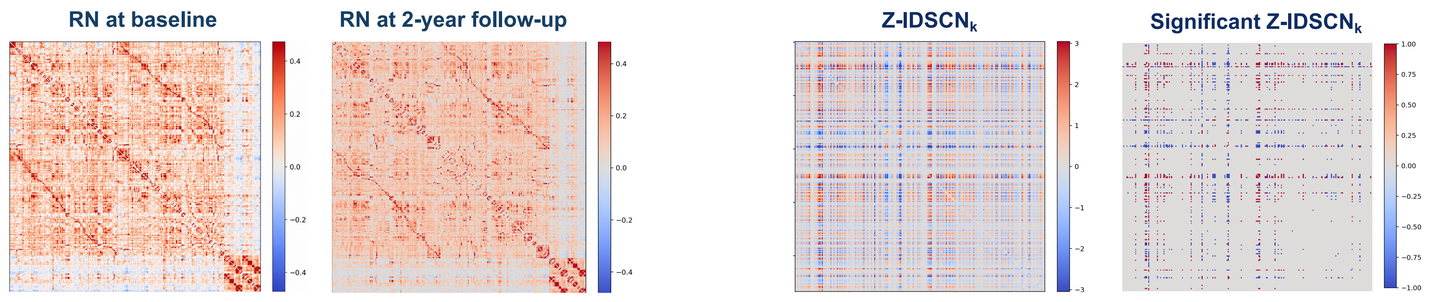
RN: reference covariance network

PN: perturbed covariance network

IDSCN: individual defferential structural covariance netwrok

Key findings

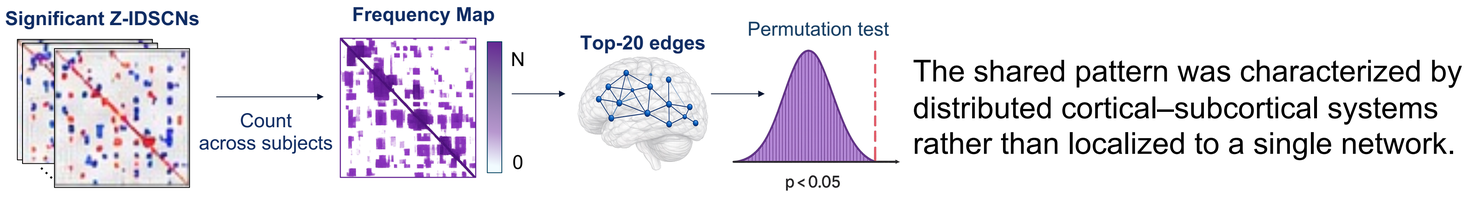
- Reference networks showed high stability across resampling procedures
- Individual structural covariance deviations were reliably detectable beyond normative perturbation levels, demonstrating that IDSCN can capture inter/intra individual differences among children with SD.



Aim 2:

Shared Structural Covariance Alterations Across Children with SD

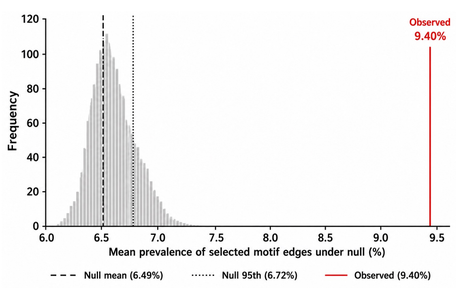
Approach



The shared pattern was characterized by distributed cortical–subcortical systems rather than localized to a single network.

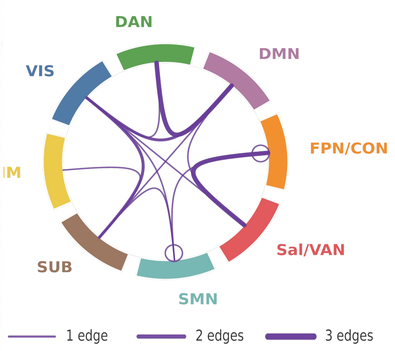
Key findings

- Despite substantial inter-individual variability, a shared pattern of structural covariance deviations emerged across children with SD. The pattern was defined by the 20 most prevalent deviation edges and was observed significantly more often than expected by chance.



Parcer i – Parcel j	Prevalence	Network Pair
lDefaultB_PFCv_2 → lSalVentAttnB_IPL_1	10.01%	DMN – Sal/VAN
lDefaultA_pCunPCC_1 → lVisPeri_StriCal_1	9.77%	DMN – VIS
lSomMotB_Cent_2 → rSomMotA_9	9.53%	SMN – SMN
lSomMotA_1 → lVisPeri_StriCal_1	9.53%	SMN – VIS
lSalVentAttnB_IPL_1 → rContA_IPS_2	9.53%	Sal/VAN – FPN/CON
lDefaultA_pCunPCC_1 → rDorsAttnA_TempOcc_1	9.45%	DMN – DAN
rVisCent_ExStr_3 → subcort_THA-DP-rh	9.45%	VIS – SUB
lContA_PFCl_2 → lSalVentAttnB_IPL_1	9.45%	FPN/CON – Sal/VAN
rDefaultA_PFCm_1 → rDorsAttnB_PostC_4	9.45%	DMN – DAN
lContC_pCun_2 → rContB_Temp_2	9.45%	FPN/CON – FPN/CON
lContA_PFCl_2 → lSomMotB_S2_2	9.29%	FPN/CON – SMN
rVisCent_ExStr_3 → subcort_aGP-rh	9.29%	VIS – SUB
lDefaultC_IPL_1 → lVisPeri_StriCal_1	9.29%	DMN – VIS
lContA_PFCl_2 → lSalVentAttnB_PFCl_1	9.29%	FPN/CON – Sal/VAN
lSomMotA_4 → subcort_mAMY-rh	9.29%	SMN – SUB
lVisPeri_StriCal_1 → rDorsAttnA_TempOcc_1	9.21%	VIS – DAN
lSalVentAttnB_PFCl_1 → lVisCent_ExStr_5	9.21%	Sal/VAN – VIS
lDefaultB_PFCd_3 → lDorsAttnB_PostC_4	9.21%	DMN – DAN
lLimbicA_TempPole_2 → subcort_mAMY-rh	9.13%	LIM – SUB
rDefaultA_PFCm_2 → subcort_pPUT-rh	9.13%	DMN – SUB

Network Contribution		
VIS:	Visual Network	7
DMN:	Default Mode Network	7
FPN/CON:	Frontoparietal / Control Network	6
Sal/VAN:	Salience / Ventral Attention Network	5
SMN:	Somatomotor Network	5
SUB:	Subcortical Network	5
DAN:	Dorsal Attention Network	4
LIM:	Limbic Network	1



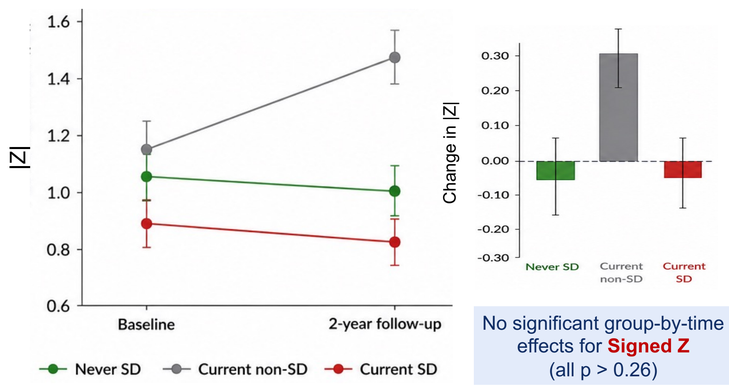
Aim 3:

Longitudinal changes of the SD-related structural covariance pattern

Model : |Z| ~ Group×Time + Pubertal stage + (1|subject) + (1|edge)

Linear mixed-effect model with random intercepts for subject and edge

Longitudinal change in |Z|	β	p
Current SD (vs never SD)	-0.003	0.86
Current non- SD (vs never SD)	0.037	0.06
Current non- SD vs Current SD	**-0.041**	**0.006**
Pubertal stage	-0.027	**<0.001**



No significant group-by-time effects for **Signed Z** (all p > 0.26)

The longitudinal changes of the shared deviation pattern differed according to current SD status

Conclusions

- Distributed alterations in brain structural covariance organization support a network-level rather than region-specific view of SD in preadolescence.
- SD history may matter: longitudinal differences in structural covariance alteration were not fully captured by current symptom status alone.

Reference

1. Lewien, C., et al., Sleep-related difficulties in healthy children and adolescents. BMC Pediatrics, 2021. 21(1): p. 82.
2. Bethlehem, R.A.I., et al., Brain charts for the human lifespan. Nature, 2022. 604(7906): p. 525-533.

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