Parcellating convergence and divergence of cortical phenotypes across autism, ADHD, and schizophrenia

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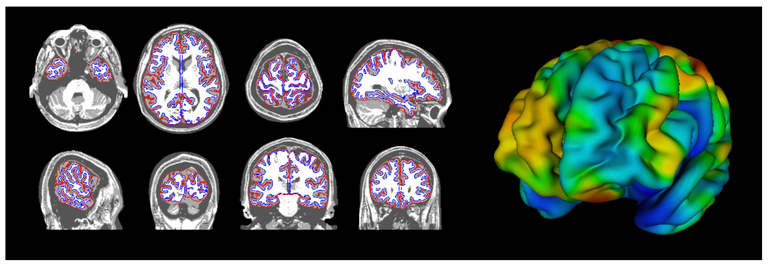
Introduction

- Neuropsychiatric disorders share common traits along a significant spectrum of genetic, neurobiological, and clinical dimensions—indicating possible shared aetiologies between disorders.
- To better understand convergent and divergent compromise to brain structure across disorders, we examined structural integrity of the cortex across ASD, ADHD, and schizophrenia,
- Test convergence and divergence at multiple hierarchical levels of information: local, global, network, and cross-modal to yield a better understanding of systematic changes across disorders.

Methods

Image processing. T1-weighted brain scans from publically available databases. Cortical thickness (CT) and surface area (SA) automatically measured using the CIVET pipeline.



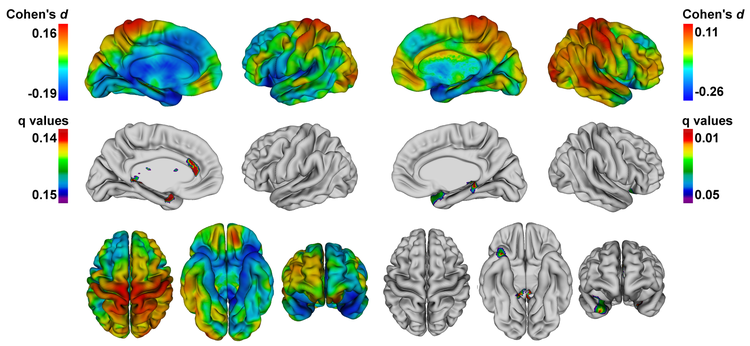
Meta analysis. Vertex-wise multiple linear regression per site, modeling effects of diagnosis on CT and SA while accounting for age and sex as covariates. Results were pooled using random effects meta-analysis, for single-disorder, paired-disorder (ASD-ADHD, ASD-SCZ, ADHD-SCZ), and combined (all three disorders).

Cross-disorder comparisons. Effect size distributions examined for skew, spatial similarity using Pearson's r of -log(p values). Correlations between disorders measured for both global and network-constrained brain regions.

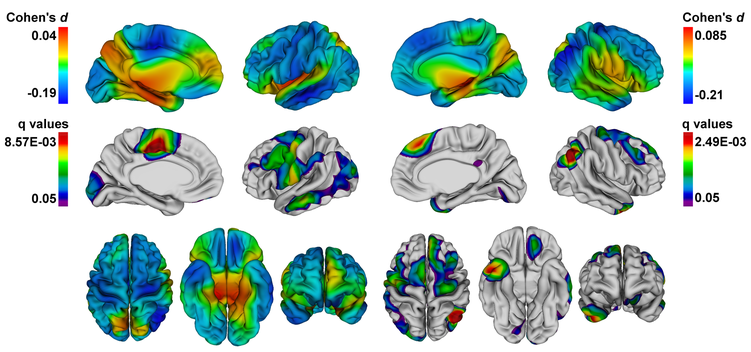
Network enrichment analysis. Adaptation of gene-set enrichment analysis (GSEA) statistics to detect systemic, network-wide structural alterations within resting state networks.

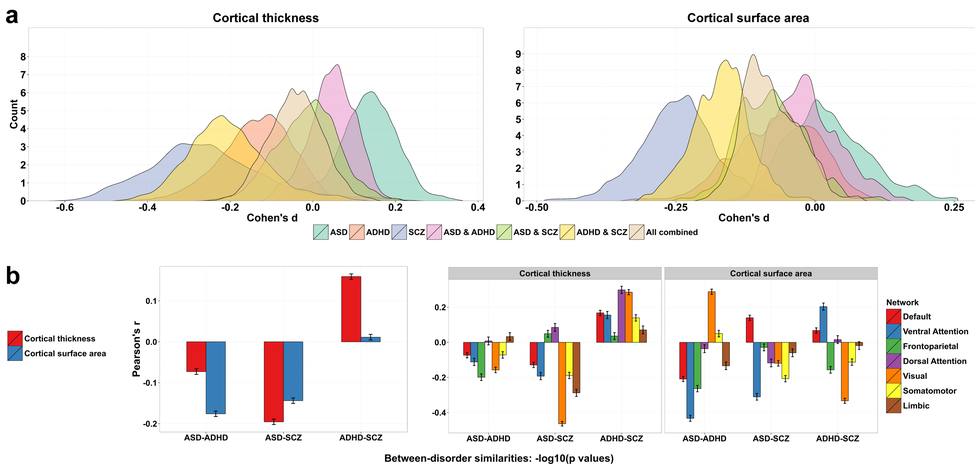
Results

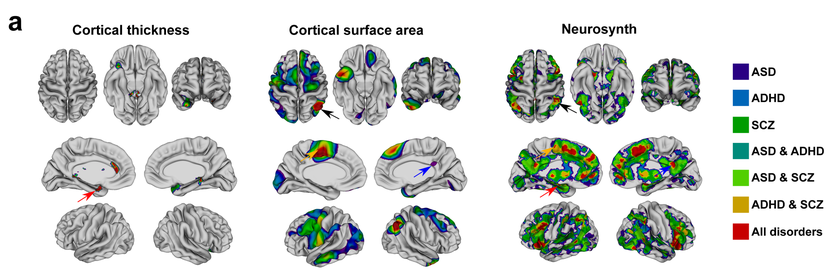
Cortical thickness



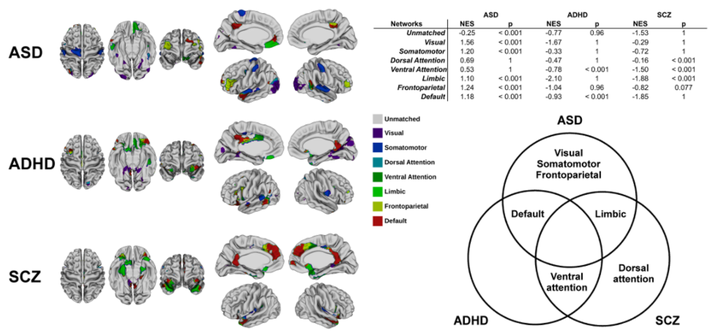
Cortical surface area





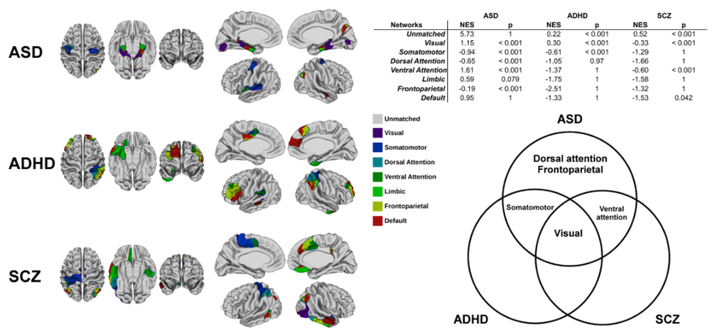


Cortical thickness



Networks	ASD NES	ASD p	ADHD NES	ADHD p	SCZ NES	SCZ p
Unmatched	-0.25	< 0.001	-0.77	0.96	-1.53	1
Visual	1.56	< 0.001	-1.67	1	-0.29	1
Somatomotor	1.20	< 0.001	-0.33	1	-0.72	1
Dorsal Attention	0.69	1	-0.47	1	-0.16	< 0.001
Ventral Attention	0.53	1	-0.78	< 0.001	-1.50	< 0.001
Limbic	1.10	< 0.001	-2.10	1	-1.88	< 0.001
Frontoparietal	1.24	< 0.001	-1.04	0.96	-0.82	0.077
Default	1.18	< 0.001	-0.93	< 0.001	-1.85	1

Cortical surface area



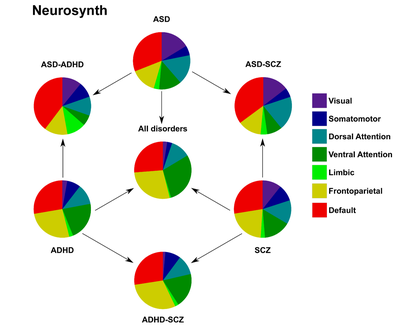
Networks	ASD NES	ASD p	ADHD NES	ADHD p	SCZ NES	SCZ p
Unmatched	5.73	1	0.22	< 0.001	0.52	< 0.001
Visual	1.15	< 0.001	0.30	< 0.001	-0.33	< 0.001
Somatomotor	-0.94	< 0.001	-0.61	< 0.001	-1.29	1
Dorsal Attention	-0.65	< 0.001	-1.05	0.97	-1.66	1
Ventral Attention	1.61	< 0.001	-1.37	1	-0.60	< 0.001
Limbic	0.59	0.079	-1.75	1	-1.58	1
Frontoparietal	-0.19	< 0.001	-2.51	1	-1.32	1
Default	0.95	1	-1.33	1	-1.53	0.042

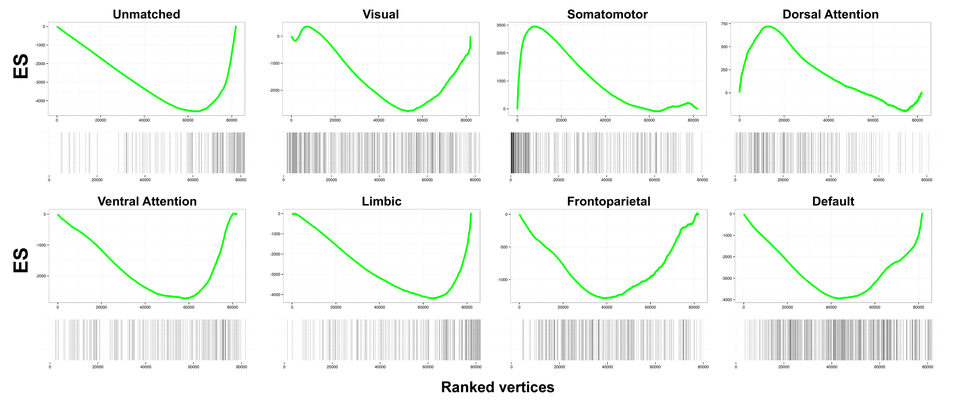
Cortical thickness

Networks	ASD & ADHD NES	ASD & ADHD p	ASD & SCZ NES	ASD & SCZ p	ADHD & SCZ NES	ADHD & SCZ p	All disorders NES	All disorders p
Unmatched	-0.93	< 0.001	-5.45	< 0.001	-1.53	1	-3.81	1
Visual	1.22	< 0.001	0.83	< 0.001	-0.65	< 0.001	-0.85	< 0.001
Somatomotor	1.79	< 0.001	3.41	< 0.001	-0.41	< 0.001	1.19	< 0.001
Dorsal Attention	1.14	< 0.001	1.62	< 0.001	-0.15	1	0.42	< 0.001
Ventral Attention	0.62	1	-1.80	1	-1.19	1	-1.41	1
Limbic	-0.41	< 0.001	-2.71	0.45	-2.25	< 0.001	-2.40	1
Frontoparietal	1.14	< 0.001	-0.32	1	-0.99	0.34	-0.57	< 0.001
Default	1.19	< 0.001	-1.04	0.91	-1.54	0.95	-1.04	0.98

Cortical surface area

Networks	ASD & ADHD NES	ASD & ADHD p	ASD & SCZ NES	ASD & SCZ p	ADHD & SCZ NES	ADHD & SCZ p	All disorders NES	All disorders p
Unmatched	5.64	< 0.001	0.45	< 0.001	0.71	< 0.001	0.44	< 0.001
Visual	-1.34	1	-1.40	1	0.66	< 0.001	-1.01	0.68
Somatomotor	-1.59	0.9	-1.81	1	-0.44	< 0.001	-1.29	1
Dorsal Attention	-1.25	1	-1.71	1	-0.89	< 0.001	-1.42	1
Ventral Attention	-1.11	1	-0.72	< 0.001	-1.46	1	-1.03	0.91
Limbic	-1.32	1	-0.82	< 0.001	-2.12	1	-1.07	1
Frontoparietal	-1.82	0.07	-1.14	1	-2.79	< 0.001	-1.58	1
Default	-0.88	< 0.001	-0.76	< 0.001	-2.03	< 0.001	-0.97	0.02





Conclusions

- Limited local anatomical, mixed global, greater network-wide, and some cross-modal convergence.
- Our understanding, or at least the approach to analysis, of altered neuroanatomy in psychiatric disorders has traditionally focused on reduced grey matter and/or gyrification in distinct regions. However—we show that by studying multiple psychiatric disorders simultaneously, patterns of altered brain structure cannot be described as simple reductions or increases of MRI-derived metrics of cortical topology.
- Instead, we find that much of these deficits across disorders may arise through coordinated, wide-spread alterations across distributed regions that participate in functional networks responsible for dynamic cortical processing of complex human traits.

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