Cortical structural changes of Morphometric INverse Divergence network in autism spectrum disorder and their associated transcriptional signatures

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Highlights

- **Cortical morphometric alterations identified in ASD via MIND network analysis.**
- **Topological network disruptions reveal atypical connectivity in ASD.**
- **Transcriptomic signatures linked to structural changes in ASD suggest neurodevelopmental dysregulation.**

Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by impaired social communication and repetitive behaviors.

Structural brain changes in ASD have been well documented, but there is a need to investigate these changes from a network perspective.

The **Morphometric Inverse Divergence (MIND)** network is a novel computational tool designed to assess structural similarity between brain regions based on multivariate MRI features.

This study applies MIND network analysis to examine cortical morphometric changes in ASD individuals, integrating these results with brain-wide gene expression data from the Allen Human Brain Atlas (AHBA).

By combining network-based morphometry with transcriptomic data, this study aims to provide new insights into the molecular mechanisms underlying cortical dysconnectivity in ASD.

Methods

We utilized data from the Autism Brain Imaging Data Exchange (ABIDE) dataset, which includes MRI scans from 561 ASD and 723 healthy controls (HC).

The MIND network was generated for each subject by calculating the divergence between cortical regions based on multiple MRI-derived morphological features, producing a connectivity matrices (*Destrieux atlas*). These matrices were then averaged across groups (ASD vs. HC) to examine network-level differences in structural morphology.

Partial least square regression analysis was performed to identify genes whose expression patterns were associated with altered brain connectivity in ASD.

Results

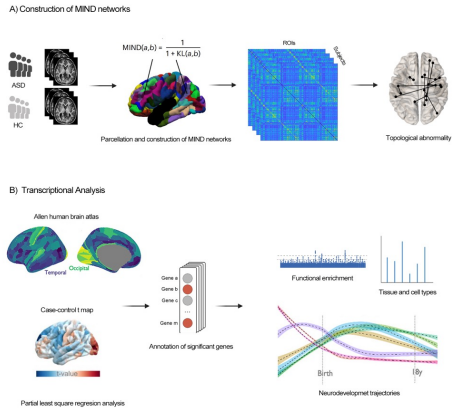

Figure 1. Schematic overview of the study. A) Multiple macrostructural features constructed the 148 × 148 matrix for MIND. B) Partial least square regression was used to identify imaging transcriptomic associations. MIND, Morphometric Inverse Divergence. ASD, autism spectrum disorder; HC, healthy control.

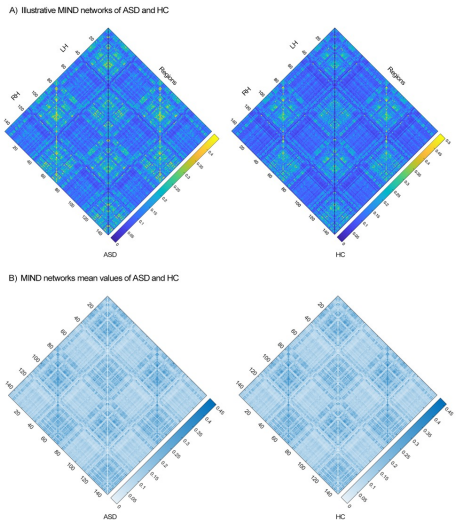

Figure 2. Cortical similarity connectomes: ASD and HC MIND networks compared. A) Illustrative MIND networks of ASD and HC. B) Mean values of the MINID values. LH, left hemisphere; RH, right hemisphere; MIND, Morphometric Inverse Divergence. ASD, autism spectrum disorder; HC, healthy control.

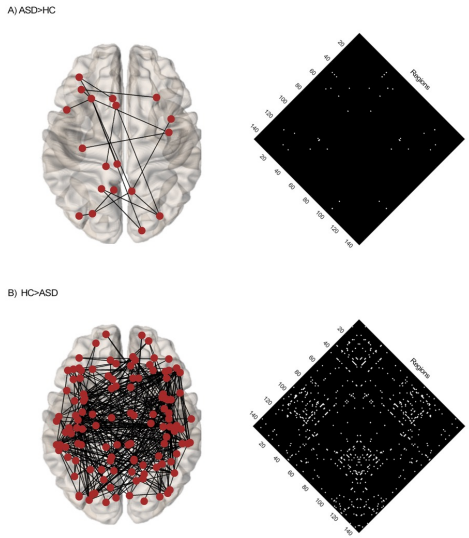

Figure 2. Group comparisons of the connections of the MIND networks. The figures exhibit the significant connections after the adjustment with the False Discover Rate (FDR) statistic: **A)** healthy controls>individuals with ASD and **B)** healthy controls<individuals with ASD. The adjacency matrices show the significant network nodes in a binary setting. MIND, Morphometric Inverse Divergence. ASD, autism spectrum disorder; HC, healthy control.

Conclusion and future directions

This study provides new insights into the structural and molecular dysconnectivity observed in ASD. The MIND network analysis revealed widespread cortical alterations that are reflective of disrupted integration and segregation in the ASD brain.

These structural changes were associated with gene expression patterns linked to synaptic function and neurodevelopment, suggesting that dysregulated molecular pathways may contribute to altered brain network organization in ASD.

Future research should focus on further refining the topological analysis of ASD brain networks, particularly by applying advanced graph theoretical metrics to better understand how local and global network alterations relate to behavior.

Investigating the temporal dynamics of network changes using longitudinal imaging and gene expression data may also provide insight into how dysconnectivity evolves across development in ASD.

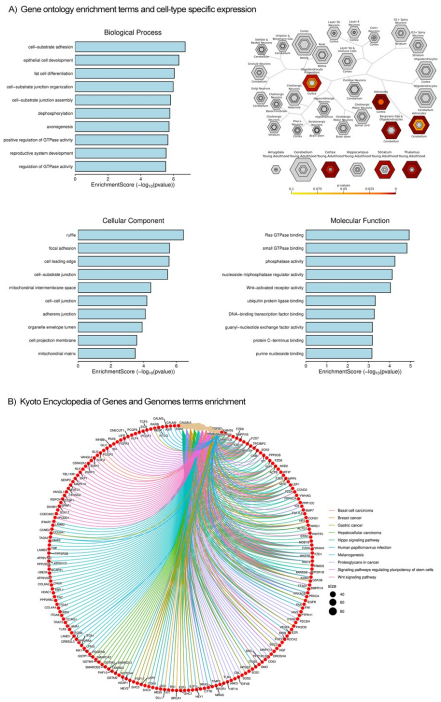

Figure 4. Transcriptomic Signatures. A) Gene ontology terms showed in bar plot with their enrichment score. In the cell type specific expression analysis, the outer hexagons correspond to the least specific test for a cell types, whereas the innermost hexagon reflects the most specific test for a cell type. **B)** The significantly enriched Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways illustrated in gene-concept network plot.

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September 2024