NeuroImage: Clinical

Volume 30, 2021, 102583

Gray matter abnormalities follow non-random patterns of co-alteration in autism: Meta-connectomic evidence

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Highlights

- We present an innovative connectomic approach based on voxel-based morphometry (VBM) meta-data.
- We mapped the topological configuration of gray matter abnormalities in autism spectrum disorder (ASD).
- ASD co-alteration network tends to overlap with the pathways of structural brain connectivity.
- Recognizable cerebral pathological hubs were captured by graph-analysis.
- A core sub-network was identified, which provides insight into our understanding of ASD.

Abstract

Background

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by atypical brain anatomy and connectivity. Graph-theoretical methods have mainly been applied to detect altered patterns of white matter tracts and functional brain activation in individuals with ASD. The network topology of gray matter (GM) abnormalities in ASD remains relatively unexplored.

Methods

An innovative meta-connectomic analysis on voxel-based morphometry data (45 experiments, 1,786 subjects with ASD) was performed in order to investigate whether GM variations can develop in a distinct pattern of co-alteration across the brain. This pattern was then compared with normative profiles of structural and genetic co-expression maps. Graph measures of centrality and clustering were also applied to identify brain areas with the highest topological hierarchy

and core sub-graph components within the co-alteration network observed in ASD.

Results

Individuals with ASD exhibit a distinctive and topologically defined pattern of GM co-alteration that moderately follows the structural connectivity constraints. This was not observed with respect to the pattern of genetic co-expression. Hub regions of the co-alteration network were mainly left-lateralized, encompassing the precuneus, ventral anterior cingulate, and middle occipital gyrus. Regions of the default mode network appear to be central in the topology of co-alterations.

Conclusion

These findings shed new light on the pathobiology of ASD, suggesting a network-level dysfunction among spatially distributed GM regions. At the same time, this study supports pathoconnectomics as an insightful approach to better understand neuropsychiatric disorders.