Anomalous Anatomical Connectivity Networks in Children with Autism Spectrum Disorder

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Abstract

Converging lines of evidence have suggested that Autism Spectrum Disorder (ASD) may be characterized by abnormal patterns of neural connectivity, with an anomalous bias towards local, versus global, connectivity.

In this study, we used Diffusion Tensor Imaging (DTI) tractography to reconstruct full-brain cortico-cortico anatomical connectivity networks in 35 children with ASD and 35 typically developing (TD) children.

We found that the anatomical connectivity neworks of children with ASD had an elevated Clustering Coefficient (CC), a measure of local interconnectivity. This indicates that children with ASD may have abmormally strong connectivity between nearby cortical regions.

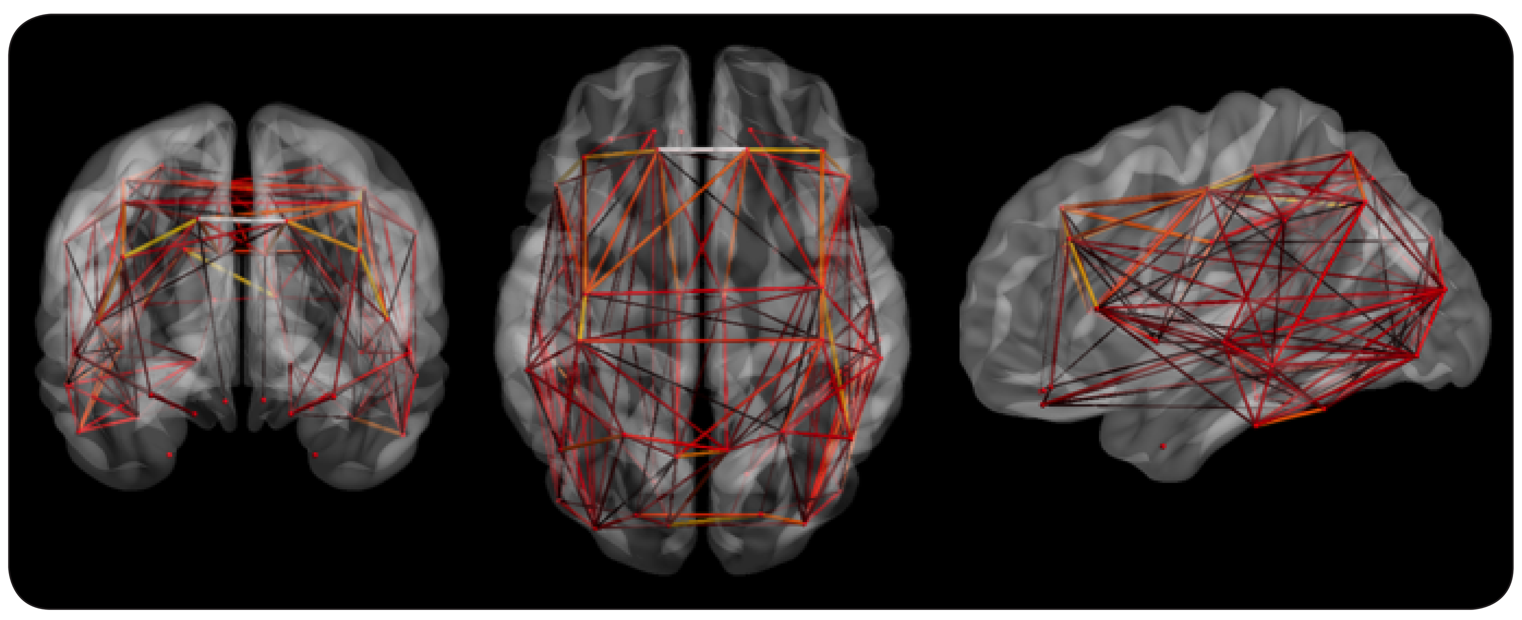
Background

Autism and Connectivity

Altered cortico-cortico connectivity has been implicated in the neurobiological basis of ASD[1] Several lines of evidence have indicated that there may be underconnectivity between distant cortical regions in ASD, and a corresponding over-expression of local connectivity[2].

Diffusion Tensor Imaging (DTI)

With DTI, we are able to measure the magnitude of water diffusion along different directions, at each point in the brain. In white matter, water diffuses faster along the white matter fibers than across them. Using this information, we can obtain the direction of the predominant white matter tract, and reconstruct course of the white matter tracts in-vivo.



An example full-brain cortico-cortico anatomical connectivity network. The brightness of the lines correspond the the strength of the connection beween the cortical regions.

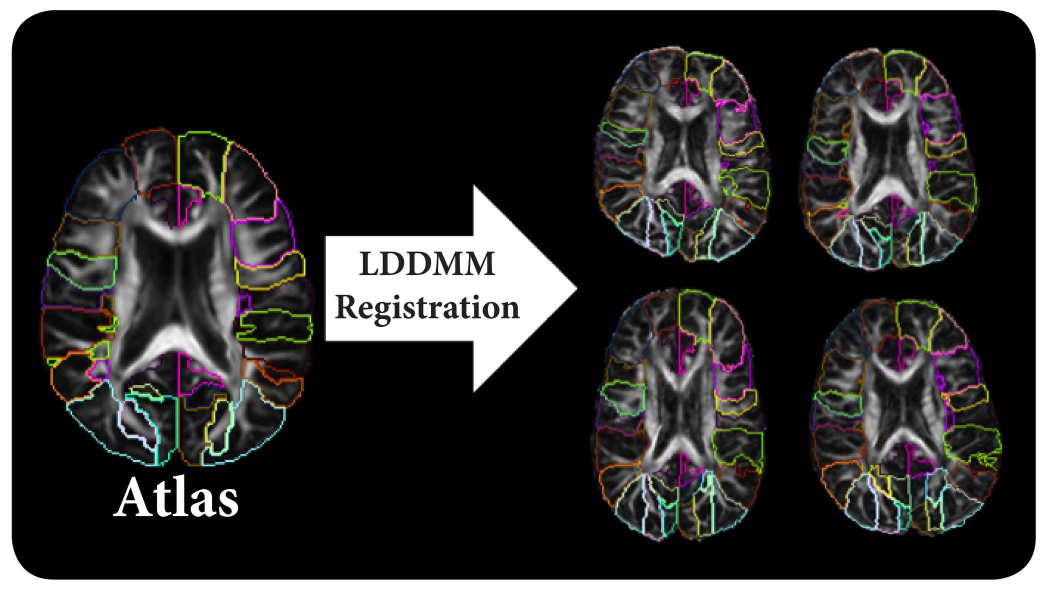
Graph Theory

Graph theory is a branch of mathematics and computer science that has recently been adapted for neuroimaging studies of whole-brain connectivity[3]. There are two principal measures that can be derived from graph theory: the Clustering Coefficient (CC) and the Characteristic Path Length (CPL). The CPL measures long-range connectivity over the whole brain. The CC looks at how interconnected each node's neighbors are with one another, and is therefore a measure of local inter-connectivity.

Our Hypothesis is that children with ASD will have a lower CPL, and a higher CC than TD controls.

Methods

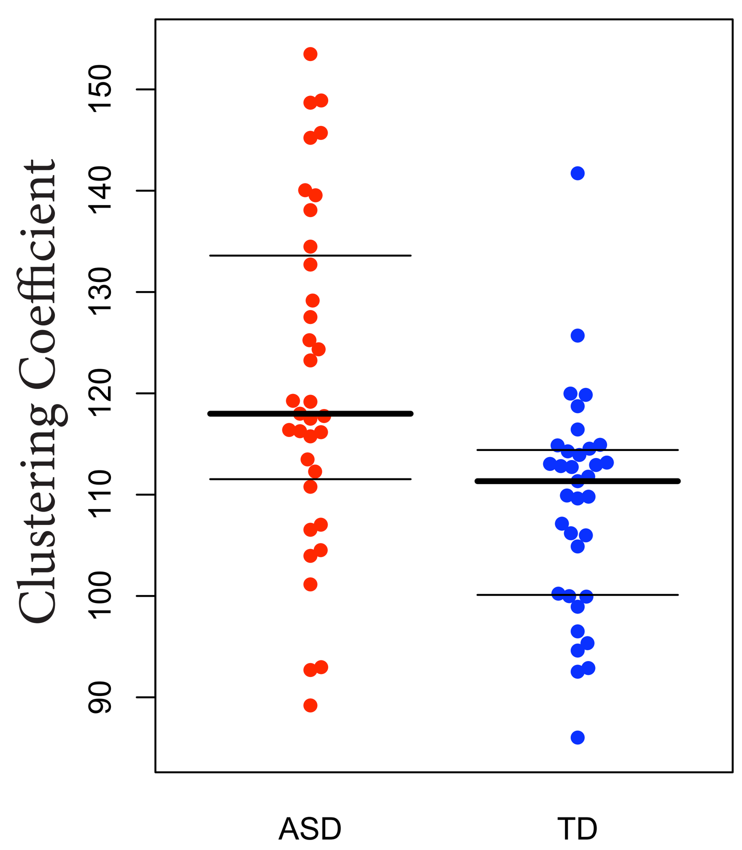
Diffusion Tensor Imaging (DTI) was collected in 35 Children with ASD, and 35 TD children, aged 9-14. The groups were matched on Age, sex, IQ and handedness. After preprocessing with CATNAP and eddy-current correction, DTI images were parcellated into cortical regions using a semi-automated atlas-based procedure[4]. Each subject's FA and B0 images were transformed to the JHU-ICBM template using multi-channel Large Deformation Diffeometric Morphic Mapping (LDDMM). The ROI labels from the JHU-ICBM atlas[5] were then back-projected onto each subject's standard-space images.



LDDMM registration is used to map the cortical regions in the atlas onto the individual subject's DTI images

Fiber-tracking was then initiated in each cortical label, using FACT as implemented in CAMINO. The number of streamlines connecting each cortical region to each other cortical region was taken as a measure of connectivity between cortical regions. Graph-theory measures (the CPL and CC) were computing using the Brain Connectivity Toolbox[6].

Results



The clustering coefficient of the full-brain anatomical networks of children with ASD was found to be significantly higher compared to typically developing controls ($p=0.0007$, rank-sum test)

The test for group difference in the characteristic path length did not reach statistical significance ($p=0.1657$)

Discussion

These findings demonstrate that graph-theoretic properties of full-brain cortico-cortico anatomical networks are sensitive to a diagnosis on the autism spectrum. This gives support to the theory that autism is associated with increased local connectivity.

Graph theory methods are well suited to investigating ASD, as they are sensitive to distruptions of the topology of the entire connectivity network, rather than investigating localized abnormalities.

References

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