Topological turning points across the human lifespan

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Abstract:

Structural topology of neural networks develops non-linearly across the lifespan and is strongly related to cognitive outcomes. Here, we aggregated diffusion imaging from nine datasets with a collective age range of zero to 90 years old (*N* = 4,216). Our analysis focused on understanding how network organization changes across age. We projected this data into a three-dimensional manifold space using Uniform Manifold Projection and Approximation. Using this manifold, we identified four major turning points in topology across the lifespan: at ages 8, 32, 62, and 85 years. These turning points demarcate five major epochs within which topological development occurs along similar trajectories. By comparing correlations, principal components analysis scores, and dynamic time warping distances, we conclude these epochs mark important shifts in topological development based on directionality, driving forces, and trajectories. Our findings underscore the significance of generalizing topological development beyond individual organizational metrics to enrich our understanding of network development trajectories and crucial turning points across the lifespan. Future directions for this project include using weighted generative network modeling and cognitive analysis to investigate potential disparities in topological trajectories among individuals.

Keywords: topology; structural networks; manifold learning; lifespan trajectories

Introduction

Structural brain networks capture the architecture underlying information exchange in the brain. The topology of these networks is associated with important cognitive outcomes (Sporns et al., 2004). Graph theory can be used to analyze network organization and to identify connection characteristics that relate to cognitive outcomes, thereby facilitating a deeper understanding the relationship between topology and cognition (Rubinov & Sporns, 2010).

Previous research has delineated topological milestones of specific organizational metrics, such as the “U” shape of development that occurs around 30 years old and is characterized by peak network efficiency and integration (Puxeddu et al., 2020; Riedel et al., 2022; Zhao et al., 2015). However, the full picture of normative topological trajectories across the lifespan, as well as their alignment with cognitive milestones, remains unknown.

Complex network topology analysis requires dimensionality reduction to identify patterns in a data-driven manner. Manifold learning is a popular method that aims to preserve the geometric structure of high-dimensional data while projecting it into a low-dimensional space (Cayton, 2008). Among manifold learning techniques is Uniform Manifold Approximation and Projection (UMAP), which captures both local and global data structures with a faster runtime compared to similar methods (e.g., t-SNE) (McInnes et al., 2018).

This study explores structural topological development across the lifespan using data-driven methods. Specifically, we: (1) investigate the relationship between age and topological integration, segregation, and centrality; (2) utilize UMAP to define a manifold space and identify major turning points across the lifespan, and (3) examine how these turning points capture significant shifts in topological trajectories.

Methods

Datasets & tractography

This project includes diffusion tensor imaging data from nine datasets that together range from zero to 90 years old (dHCP: Edwards et al., 2022; BCP: Howell et al., 2019; CALM: Holmes et al., 2019; RED: Bignardi et al., 2021; ACE: Johnson et al., 2021; HCPd: Somerville et al., 2018; HCPya: Van Essen et al., 2013; HCPa: Bookheimer et al., 2019; CamCAN: Shafto et al., 2014). Normalized weighted networks were generated with deterministic tractography (Yeh et al., 2010) using the AAL90 neonatal, one year, two year, and adult atlases (Shi et al., 2011; Tzourio-Mazoyer et al., 2002). The original sample (*N* = 4,216) was harmonized across atlas and dataset using ComBat (Fortin et al., 2017).

For analysis, only neurotypical participants were used ($N = 3{,}082$; female $n = 1{,}994$; male $n = 1{,}808$).

Network topology

Using the Brain Connectivity Toolbox (Rubinov & Sporns, 2010), we calculated 12 global and average local measures of network organization.

Manifold construction & turning points

We used Uniform Manifold Approximation and Projection (McInnes et al., 2018) to derive 968 3D manifold spaces of topological data (minimum distance = 0 – 1, nearest neighbors = 2 – 89). We ran least squares polynomial fits to derive 3D lines of best fit and used the gradients of these lines to determine major turning points in topological development (Fig. 1A).

Statistics

To explore topology across age, we used generalized additive models (controlling for sex, atlas, and dataset). LASSO regularization and Pearson correlations were used to examine topological changes within epochs (Fig. 1B). We also conducted a principal components analysis with parallel analysis on topological measures (Fig. 1C). Between epochs, we analyzed PCA scores with Welch's ANOVA and Games-Howell post-hoc test.

Results

Connectivity & Topology

Weighted networks significantly fluctuate in density – with highly density at birth and 30 years old ($p < 0.001$). However, the average strength of networks significantly increased nearly linearly across the lifespan ($p < 0.001$). Global efficiency fluctuated in the first two decades of life, with the highest point of at 28 years before steadily declining through 90 years old ($p < 0.001$). Modularity had a lifetime low at 30 years old was followed by progressive increase throughout aging ($p < 0.001$). Clustering coefficient significantly increased linearly across the lifespan ($p < 0.001$).

Lifespan Epochs

Four major turning points were identified – eight, 32, 62 and 85 years old (Fig. 1A,D). These defined five epochs which were driven by different organization properties as well as displayed significantly different correlational patterns (Fig. 1B). Early epochs are significantly different from each other in PC1 and PC2 whereas older epochs were significantly different in PC3 (Fig. 1C). Warping distances between epochs indicate trajectories between epochs two and three were the most different (distance = 4.27) compared to epochs one to two (dist. = 2.89), epochs three to four (dist. = 3.24) and epochs four to five (dist. = 2.12). Together, these turning points capture important but complex shifts in topological development (Fig. 1D).

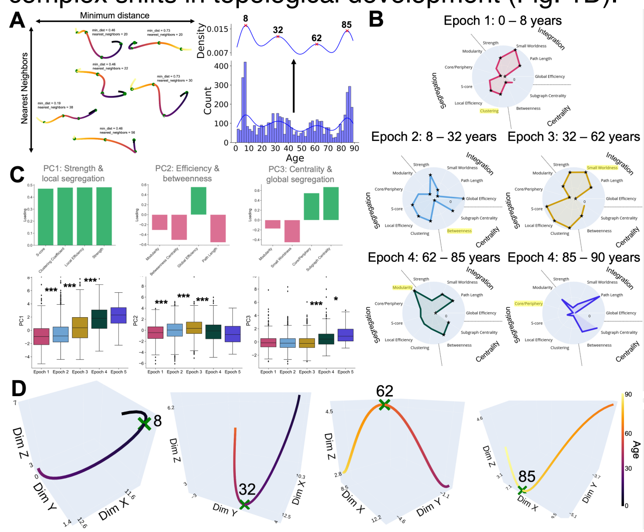

Figure 1: Lifespan topological turning points. (A) Example manifolds with turning points (green dots). Histogram and density plot of all turning points (red x indicates selected turning points). (B) Correlations with age for epoch (black stars indicate p < 0.05; highlights indicate largest LASSO coefficient). (C) Largest four PCA loadings and boxplots of PCA scores across the epochs (*** indicates p < 0.001, ** indicates p < 0.01, * indicates p < 0.05). (D) Manifold spaces for each epoch (green X indicates the turning points).

Future Directions

This research will next use weighted generative network modeling (GNM) (Akarca et al., 2023) to explore how network wiring constraints change across the lifespan and to investigate whether alterations in these economic conditions align with major turning points (Fig. 2A). Additionally, standardized fluid cognition scores will be used to delineate 'high' (85th percentile or above) and 'low' (15th percentile or below) cognitive groups (Fig. 2B). The aim of this second project is to determine if cognitive groups differ significantly in topology, turning points, or economic wiring constraints.

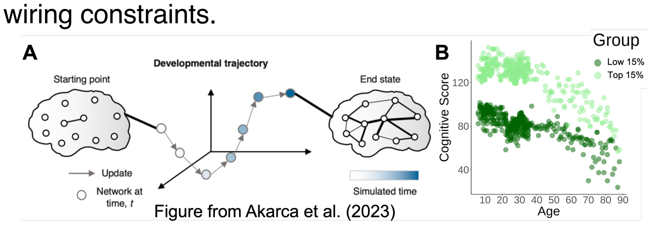

Figure 2: Future directions of the project with GNMs and cognitive subgroups. (A) Schematic by Akarca et al. (2023) outlining weighted GNMs theory. (B) Standardized fluid cognition groups which will be used to explore potential topology-cognition links across the lifespan.

Acknowledgments

We want to thank Dr Fang-Cheng Yeh for sharing fiber tracking files of many datasets on DSI Studio. Dr Yeh's analysis was conducted using the resource allocation (TG-CIS200026) at Extreme Science and Engineering Discovery Environment (XSEDE) resources (Towns, J. et al. Computing in science & engineering 16, 62-74 2014). The FIB files and tractography files are shared using Creative Commons Attribution-Share A like 4.0 International License.

We must thank all project researchers, funders and participants that have enable open access to such incredible data resources. Data was provided (1) by developing Human Connectome Project, KCL-Imperial-Oxford Consortium funded by the European Research Council under the European Union Seventh Framework Programme (FP/2007-2013) / ERC Grant Agreement no. 319456; (2) by the efforts of the University of North Carolina at Chapel Hill and The University of Minnesota (UNC/UMN) Baby Connectome Project Consortium and supported by the NIH grant (1U01MH110274); (3) by the Centre for Attention, Learning and Memory. CALM funding was provided by the UK Medical Research Council and University of Cambridge, UK (https://calm.mrc-cbu.cam.ac.uk/); (4) by the MRC Cognition and Brain Sciences Unit by the RED team; (5) by ACE at the MRC Cognition and Brain Sciences Unit and was supported by funding from the Templeton World Charity Foundation (TWCF0159) and the Medical Research Council, UK (MC-A0606-5PQ41); (6) by HCPd supported by the National Institute of Mental Health of the National Institutes of Health under Award Number U01MH109589 and by funds provided by the McDonnell Center for Systems Neuroscience at Washington University in St. Louis. The HCP-Development 2.0 Release data used in this report came from DOI: 10.15154/1520708; (7) by the Human Connectome Project, WU-Minn Consortium (Principal Investigators: David Van Essen and Kamil Ugurbil; 1U54MH091657) funded by the 16 NIH Institutes and Centers that support the NIH Blueprint for Neuroscience Research; and by the McDonnell Center for Systems Neuroscience at Washington University; (8) by HCPa supported by the National Institute on Aging of the National Institutes of Health under Award Number U01AG052564 and by funds provided by the McDonnell Center for Systems Neuroscience at Washington University in St. Louis. The HCP-Aging 2.0 Release data used in this report came from DOI: 10.15154/1520707; and (9) by the Cambridge Centre for Ageing and Neuroscience (CamCAN). CamCAN funding was provided by the UK Biotechnology and Biological Sciences Research Council (grant number BB/H008217/1), together with support from the UK Medical Research Council and University of Cambridge, UK.

A.M. is supported by the Gates Cambridge Foundation. D.E.A. is supported by Medical Research Council Program Grant MC-A0606-5PQ41 and the James S. McDonnell Foundation Opportunity Award and the Templeton World Charity Foundation, Inc. (funder DOI 501100011730) under the grant TWCF-2022-30510. This publication does not necessarily reflect the views of the funding agencies.

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