NEURO WORKSHOP

Friday, July 21 | 9 a.m. EDT

Jeanne Timmins Amphitheatre, The Neuro

GRADIENTS OF BRAIN ORGANIZATION

July 21, 2023

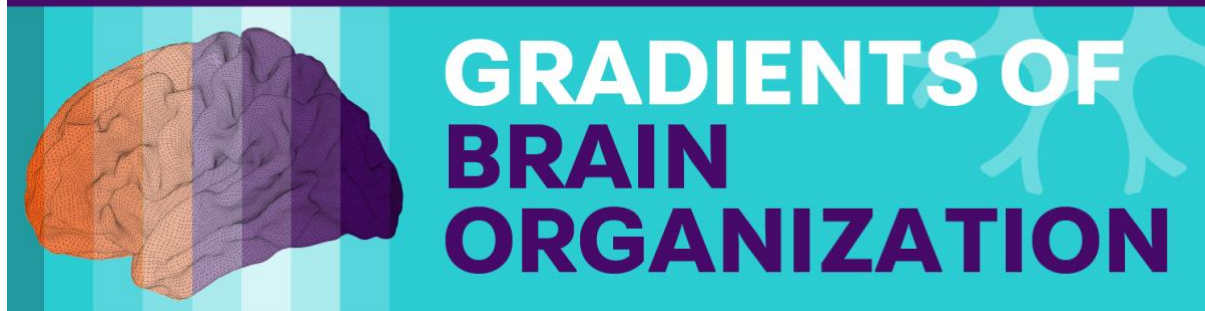## The Neuro, 3801 University Street | Jeanne Timmins Amphitheatre

Program Booklet

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Recent years have seen a rise of new methods and applications to study smooth spatial transitions — or gradients — of brain organization. Identification and analysis of cortical gradients provides a framework to study brain organization across species, to examine changes in brain development and aging, and to more generally study the interrelation between brain structure, function and cognition. In this pre-OHBM workshop, held on the 21st of July 2023, we will bring together outstanding junior and senior scientists to discuss the challenges and opportunities afforded by this emerging perspective.

Early career researchers will take centre stage for a series of talks on state-of-the-art development and application of gradient approaches, while a diverse range of established scientists from across the globe will chair the proceedings. In this manner, we hope to stimulate discussions on how gradients are changing our understanding of brain organisation and to initiate fellow researchers to this burgeoning field.

THE NEURO

The Neuro – The Montreal Neurological Institute-Hospital – is a bilingual, world-leading destination for brain research and advanced patient care. Since its founding in 1934 by renowned neurosurgeon Dr. Wilder Penfield, The Neuro has grown to be the largest specialized neuroscience research and clinical center in Canada, and one of the largest in the world. The seamless integration of research, patient care, and training of the world's top minds make The Neuro uniquely positioned to have a significant impact on the understanding and treatment of nervous system disorders. In 2016, The Neuro became the first institute in the world to fully embrace the Open Science philosophy, creating the Tanenbaum Open Science Institute. The Montreal Neurological Institute is a McGill University research and teaching institute. The Montreal Neurological Hospital is part of the Neuroscience Mission of the McGill University Health Centre. For more information, please visit www.theneuro.ca.

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PROGRAM

Jeanne Timmins Amphitheatre, The Neuro, 3801 University Street

8:30 - 9:00	Registration & Coffee
9:00 - 9:15	Welcome

9:15 - 10:30	Multiscale Studies Chairs: Konrad Wagstyl and Jessica Royer
	Tools for Multimodal, Multiscale Annotation of Brain Networks *Justine Hansen, McGill University, Canada* **Three components of human brain gene expression reflect normative developmental programmes with specific links to neurodevelopmental disorders** *Richard Dear, University of Cambridge, UK* **Organization of Laminar Thickness Covariance in the Human Cortex** *Amin Saberi, Max Planck Institute for Human Cognitive and Brain Sciences and Forschungszentrum Jülich, Germany* Panel discussion

10:30 - 10:45	Coffee break

10:45 - 12:00	Evolutionary perspectives Chairs: Sofie Valk and Ting Xu
	Gradients and The Search for Human Brain Specializations *Nicole Eichert, University of Oxford, UK* **Intrinsic Timescales as a Unifying Organizational Principle of Neural Processing in Nonhuman Primates** *Ana M. G. Manea, University of Minnesota, USA*

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Linking Temporal Lobe Organization Across Modalities to Individual Differences in Language Processing
Marius Braunsdorf, Donders Centre for Cognition, The Netherlands

Panel Discussion

12:00 - 13:00	Lunch break
13:00 - 13:15	Flash Talks
13:15 - 14:30	Dynamics Chairs: Seok-Jun Hong and Richard Bethlehem

Neural State Dynamics Along the Canonical Gradients of Functional Brain Organization Reflect Cognitive and Attentional Dynamics
Hayoung Song, University of Chicago, USA

Large-Scale Biophysical Models and Neuronal Dynamics
Shaoshi Zhang, National University of Singapore, Singapore

Gradients Go to the Movies: Macroscale Cortical Organization During Naturalistic Viewing
Tamara Vanderwal, University of British Columbia, Canada

Panel discussion

14:30 - 14:45	Coffee break
14:45 - 16:15	Cognitive and clinical perspectives Chairs: Daniel Margulies and Theodore Satterthwaite

Why Cognitive Neuroscience Needs a State Space
Bronte Mckeown, Queen's University, Canada

Cortical Gradients in Semantic Cognition
Tirso Gonzalez-Alam, University of York, UK

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Atypical Functional Connectivity Subspaces Reflect Declarative Retrieval Impairments in Temporal Lobe Epilepsy
Donna Gift Cabalo, McGill University, Canada

Structure-Function Plasticity Coupling for Improved Perceptual Decisions
Liz Yuanxi Lee, University of Cambridge, UK

Panel Discussion

16:15 - 16:45	Closing comments
16:45 - 17:00	Transition
17:00 - 18:30	Poster session and cocktail

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SPEAKER, HOST & CHAIR BIOGRAPHIES

Amin Saberi

Amin Saberi is a PhD student at the Cognitive Neurogenetics Lab led by Dr. Sofie Valk and situated at the Max Planck Institute for Human Cognitive and Brain Sciences and Research Center Jülich (INM-7). Previously, he has studied medicine at the Mashhad University of Medical Sciences (2011-2019), followed by a research stay at the Institute of Medical Science and Technology at Shahid Beheshti University (2019-2021). His research is focused on using computational neuroscience techniques on neuroimaging data to study the low-dimensional structural and functional properties of the brain and their links to behavior and psychiatric disorders. He is also interested in open and reproducible science, as well as developing and improving tools for analyzing brain data.

Ana M.G. Manea

Ana Manea is a PhD Candidate at the University of Minnesota working at the Center for Magnetic Resonance Imaging under the supervision of Dr. Jan Zimmermann. Her work combines ultra-high field magnetic resonance imaging and electrophysiology to study whole-brain temporal and spatial dynamics in nonhuman primates.

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Bronte Mckeown

Bronte is a postdoctoral fellow at Queen's University in the ThinC Lab run by Professor Jonathan Smallwood. She is interested in understanding how our brains and the world around us shape our thoughts and how our thoughts shape our lives.

Daniel Margulies

Daniel Margulies leads the Cognitive Neuroanatomy Lab based at the Integrative Neuroscience & Cognition Center (INCC – UMR 8002) at the University of Paris and Centre national de la recherche scientifique (CNRS) as well as the Wellcome Centre for Integrative Neuroimaging at Oxford University. The Cognitive Neuroanatomy Lab investigates principles of how the cerebral cortex is spatially organized and the role of that organization in human cognition.

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Donna Gift Cabalo

Donna Gift Cabalo is a Ph.D. Trainee at McGill University under Dr. Boris Bernhardt's supervision. She holds an impressive academic record with a cum laude bachelor's and master's degree from the University of Trento, where she received the prestigious MAECI fellowship from the Italian Government. Ms. Cabalo joined the MICA lab at the MNI in January 2022, focusing on profiling memory networks in temporal lobe epilepsy patients. Her research involves applying advanced data science techniques to functional neuroimaging data, including MRI data acquired at high and ultra-high field strengths. By studying memory network organization and reorganization in patients with mesiotemporal lesions, her work aims to identify novel biomarkers and predict post-operative memory deficits for pharmaco-resistant TLE patients undergoing epilepsy surgery. She receives funding from the Canada First Research Excellence Fund, Fonds de recherche du Québec, awarded to Healthy Brains, Healthy Lives initiative at McGill University, and the IPN Excellence Award in Neurology and Neurosurgery.

Hayoung Song

Hayoung is a cognitive neuroscientist and a PhD student at the University of Chicago working with Monica Rosenberg. Hayoung's research focuses on understanding neural dynamics and computations underlying real-world cognition. She uses naturalistic tasks in human behavioral and fMRI studies to study how we comprehend, engage with, and remember narratives. Hayoung investigates how functional brain systems reconfigure during cognitive and attentional state fluctuations, and the ways systems-level dynamics interact with information processing at local brain circuits.

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Jessica Royer

Jessica Royer is a clinical neuropsychologist currently pursuing her Ph.D. studies in the Integrated Program in Neuroscience at McGill University. Her research focuses on socio-affective networks in healthy and epileptic brains using multimodal MRI and electrophysiology, specifically high-density scalp EEG and intracranial recordings. Her work at the MNI is co-supervised by Dr. Birgit Frauscher and Dr. Boris Bernhardt.

Justine Hansen

Justine Hansen is a PhD student in neuroscience with Professor Bratislav Misic at the Montreal Neurological Institute. Her work is centred on bridging the microscale and macroscale in human brain networks. She is also a frequent user, contributor, and proponent of Open Science.
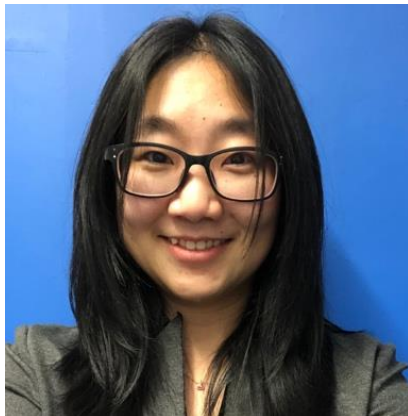
Konrad Wagstyl

Konrad is a Sir Wellcome Research Fellow at the Wellcome Centre for Human Neuroimaging, UCL, using computational methods to find links between cortical microstructure and *in vivo* neuroimaging.

As part of this work he co-leads the Multicentre Epilepsy Lesion Detection project, an open science collaboration to develop machine learning algorithms to automatically subtle focal cortical dysplasias in patients round the world.

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Liz Yuanxi Lee

Liz (Yuanxi) Lee is a research associate in Department of Psychology at University of Cambridge. Liz's research focuses on understanding the role of learning and brain plasticity. She combines behavioural paradigms, neuroimaging and genetic expressions with multimodal brain imaging methods to study the young and healthy ageing brain to understand learning and cortical plasticity across the lifespan. Liz's work also involves the interface of AI and brain science. Specifically, her research aims at translating predictive models for early neurodegenerative disease based on machine learning approaches to clinical applications. Liz received her PhD from Department of Psychology, Beijing Normal University and M. Eng from Department of Electrical Engineer, Tsinghua University. She was a visiting scholar at Wellcome Centre Integrative Neuroimaging, University of Oxford during her PhD. Her PhD work focused on understanding semantic representation in the human brain with behavioural paradigms and MRI imaging.

Marius Braunsdorf

Marius started in the Neuroecology Lab when he did his MSc research on a project on social sequential evidence accumulation as a part of his research Master in Brain and Cognitive Sciences. His project was supervised by Rogier Mars and Nils Kolling. The question of how we reach decisions for ourselves, and others forms a substantial part of being a functioning human being and defines us as social animals to a large extent. "This study of how our brain monitors who possesses which evidence at what time tackles this endeavour in a well-controlled experimental environment. Functional imaging of brain function as well as modelling of these processes shed light on how we make decisions in a social context." Following this project, Marius is currently working as a PhD student, supervised jointly by Rogier and Harold Bekkering.

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Nicole Eichert

Nicole Eichert is a Wellcome Trust postdoctoral fellow at the Wellcome Centre for Integrative Neuroimaging (WIN, University of Oxford) and a Junior Research Fellow at The Jesus College. With her research programme, Nicole wants to understand how our brain anatomy evolved to support uniquely human cognition. To answer this question, she combines magnetic resonance imaging and histology to study how the brains of different primate species differ. Nicole gained her DPhil degree in Neuroscience from the University of Oxford on a scholarship by the Wellcome Trust. After her PhD she worked for one year as Biomarker Scientist in a MedTech company. As part of her postdoctoral fellowship, Nicole collaborates with the Montreal Neurological Institute at McGill University.

Richard Bethlehem

Richard Bethlehem is the director of neuroimaging at the Autism Research Centre and assistant professor of neuroinfomatics in the department of Psychology. His work focuses on understanding lifespan changes in brain development and ageing from big data neuroimaging. In addition, his group develops tools to integrate large scale neuroimaging data with genetics and transcriptomics in an effort to better understand the biological mechanisms driving brain maturation. He collaborates closely with the BCG and Gandal labs at UPenn, the MICA lab at the MNI and the Cognitive Neurogenetics group at the MPI.

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Richard Dear

Richard Dear is a PhD student at the Brain Mapping Unit supervised by Petra Vertes and Ed Bullmore. He is interested in using computational techniques to understand the neurobiology of mental health, with a particular focus on revealing the underlying biological subtypes of depression and depressive symptoms, and identifying potential clinical biomarkers and targets for treatment. He is also broadly interested in the philosophy of neuroscience and the role of computation and theory in understanding the brain. His first degree was in physics, but with two statistics professors for parents, he initially had no intention of being in academia. He instead worked for two start-ups based in China, then ironically became a data scientist at Airbnb in San Francisco, before accepting his fate and coming to this most ivory of towers in Cambridge to pursue neuroscience.

Seok-Jun Hong

Seok-Jun Hong, PhD, is a research scientist in the Center for the Developing Brain at the Child Mind Institute. Dr. Hong's previous research has focused on advanced *in-vivo* magnetic resonance imaging of atypical brain development such as cortical malformations and autism spectrum disorders. Building upon expertise in computer science, statistics and neuroinformatics, he developed original approaches to quantitatively describe pathological neurodevelopment, such as automatic epileptogenic lesion detection and multidimensional neuroanatomical subtyping of autism. With such novel approaches, Dr. Hong yielded several high-profile studies in medical imaging and clinical neuroscience journals such as *Brain*, *Neurology* and *NeuroImage*, and also has received many research fellowships from Canada.

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Shaoshi Zhang

Shaoshi Zhang is currently a PhD student at the National University of Singapore, where he is conducting research under the supervision of Professor Thomas Yeo. His primary research interests include dynamical models, neurodevelopment, fMRI pre-processing and applications of machine learning techniques to brain imaging. His current study focuses on applying large-scale circuit model to uncover the brain maturational changes related to neurodevelopment and cognition. Shaoshi's work has also been featured in the OHBM 2023 educational course.

Sofie Valk

Sofie studied AI and philosophy before turning to the brain. She completed a PhD in social neuroscience for which she received the prestigious Otto Hahn medal and award. Following she studied genetic neuroimaging in her postdoc at Heinrich Heine University Duesseldorf. Currently she is a group leader of the 'Cognitive neurogenetics' group at Max Planck Institute for Human Cognitive and Brain Sciences in Leipzig, Germany and Forschungszentrum Juelich. Here, Sofie and her team study the interplay of genes and environment upon to brain to understand how the brain supports human cognition.

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Tamara Vanderwal

Tammy Vanderwal is a child and adolescent psychiatrist whose research focuses on the use of movies to study brain responses to complex stimuli. Her lab creates, tests and shares movies to evoke specific symptoms and types of processing during fMRI scanning, with a focus on child psychiatric disorders. She attended medical school and completed residency and fellowship training at Yale University. She is currently an assistant professor at the University of British Columbia, and a clinician scientist at the BC Children's Hospital Research Institute. She also continues to practice as a psychiatrist, providing telehealth care for children and families in remote northern communities through BC Children's Hospital.

Theodore Satterthwaite

Ted is the McLure Associate Professor in Psychiatry & Behavioral Research at the University of Pennsylvania Perelman School of Medicine. Ted completed medical and graduate training at Washington University in St. Louis, where he was a student of Randy L. Buckner. Subsequently, he was a psychiatry resident and a neuropsychiatry fellow at Penn, under the mentorship of Raquel E. Gur. He joined the faculty of the Department of Psychiatry in 2014, and served as the Director of Imaging Analytics of the Brain Behavior Laboratory from 2015-2019. Since 2020, he has directed PennLINC. His research uses multi-modal neuroimaging to describe both normal and abnormal patterns of brain development, in order to better understand the origins of neuropsychiatric illness. He has been the PI of nine R01s from NIH. His work has been recognized with the Brain and Behavior Research Foundation's Klerman Prize for Clinical Research, the NIMH Biobehavioral Research Award for Innovative New Scientists (BRAINS) award, the NIH Merit Award, as well as several teaching awards.

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Ting Xu

Ting Xu, PhD, is a research scientist in the Center for the Developing Brain at the Child Mind Institute. Her research focuses on investigating the brain connectome in human and non-human primates via various mathematical/statistical methods and applying them to investigate brain changes associated with normal brain development and those caused by disorders. She is currently on the Senior Research Scientist Track, a tenure-track equivalent at the Child Mind Institute. Recently, she has placed a growing emphasis on parcellation methodologies for characterizing cortical areal organization based upon functional MRI and understanding issues related to inter-individual variation and reliability in human and non-human primates (NHP). She has also participated in the organization, sharing and analysis of open large-scale neuroimaging datasets in human and NHP (i.e., Consortium for Reliability and Reproducibility [CoRR], and the non-human PRIMatE Data Exchange [PRIME-DE]).

Tirso RJ Gonzalez Alam

Tirso RJ Gonzalez Alam received his PhD in Cognitive Neuroscience and Neuroimaging from the University of York (February 2020), and his MSc in Clinical Neuropsychology from the National Autonomous University of Mexico. He has worked as a neuroscience research fellow, associate lecturer and clinical neuropsychologist over the last 10 years, and is currently working as a research associate in the Department of Psychology at the University of York, in the FLEXSEM lab with Professor Beth Jefferies. He is interested in understanding the neural bases of hemispheric differences in language/semantics, and believes that large-scale cortical networks and gradient decomposition techniques are a very promising avenue to achieve this. His main recent research tools have been fMRI (both task-based and resting-state), gradient decomposition, multivariate analyses, DTI tractography, cognitive paradigms, automated meta-analytical techniques and cognitive decoding.

Sara Larivière

Sara is a CIHR Banting Postdoctoral Fellow at the Center for Brain Circuit Therapeutics, Brigham and Women's Hospital, Harvard Medical School in Boston. Sara's research focuses on the development of advanced MRI techniques to study multiscale neural associations as well as leveraging big data to study network alterations in health and disease.
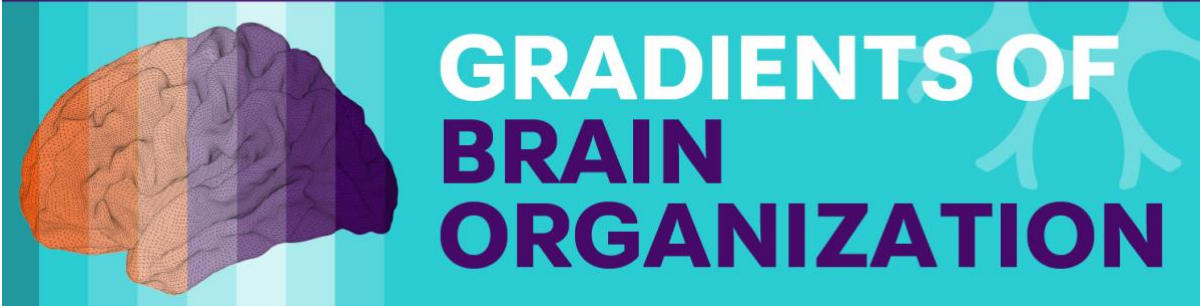
SPEAKER ABSTRACTS

Linking Temporal Lobe Organization Across Modalities to Individual Differences in Language Processing

Marius Braunsdorf, Donders Centre for Cognition, The Netherlands

We applied la placian eigenmapping to meta analytical functional activation maps to shed light on the temporal lobe's functional organisation in the light of multiplicity. A similar approach has been used by Blasquez Freches and colleagues (2021) on the temporal lobe's structural organization, focusing on connectivity using diffusion weighted imaging. We present an approach to compare similarities and differences between organizational principles found with different modalities in the temporal lobe. We account for spatial autocorrelation by creating surrogate brain maps following Burt et al.'s (2021) approach. After creating those surrogate maps, we formally compare them with an independent component analysis, similar to Nozais et al. (2021). This way we can formalize differences in organizational principles across modalities. By comparing structural and functional organization we can assess in how far the claim that function follows structure holds true in the face of structural and functional multiplicity.

Three components of human brain gene expression reflect normative developmental programmes with specific links to neurodevelopmental disorders
Richard Dear, University of Cambridge, UK

Human brain organisation emerges from the coordinated transcription of thousands of genes, and the first principal component (C1) of spatial whole genome expression was shown to reflect cortical hierarchy. Here, optimised processing of the Allen Human Brain Atlas revealed two new components of brain transcription, C2 and C3, which are distinctively enriched for neuronal, metabolic and immune processes, cell-types and cytoarchitecture, and genetic variants associated with intelligence. Using additional datasets (Allen Human Cell Atlas and BrainSpan), we found that C1-C3 represent generalisable transcriptional programmes that are coordinated within cells, and differentially phased during foetal and postnatal development. Autism spectrum disorder and schizophrenia were specifically associated with C1/C2 and C3, respectively, across neuroimaging, gene expression, and genome-wide association studies. Evidence converged especially in support of C3 as a normative transcriptional programme for adolescent brain development, which can lead to atypical supragranular brain connectivity in people at high genetic risk for schizophrenia.

Gradients and the Search for Human Brain Specializations
Nicole Eichert, University of Oxford, UK

Atypical Functional Connectivity Subspaces Reflect Declarative Retrieval Impairments in Temporal Lobe Epilepsy
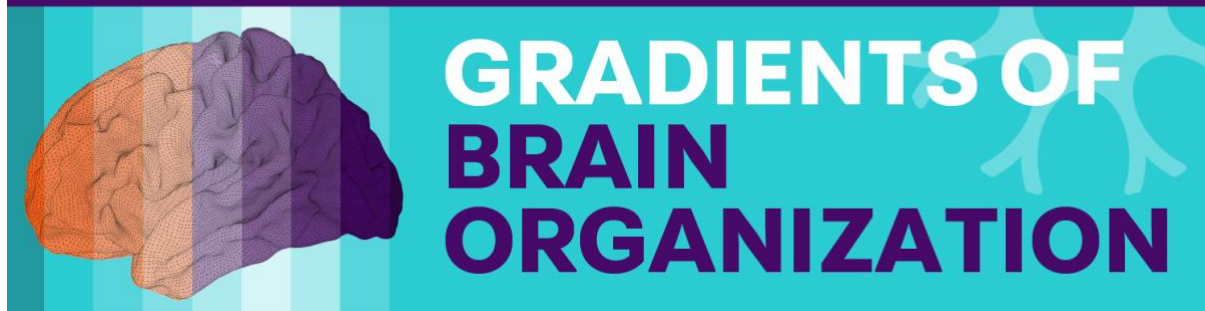Donna Gift Cabalo, McGill University, Canada

Gradients provide axes of cortical structure organization and characterize how topological features of the cortex scaffold functional hierarchies. Gradients have shown promise in mapping subregional hippocampal organization and in describing macroscale neocortical function. My talk will show an application of gradients as an analytical and conceptual framework to investigate declarative memory networks in healthy individuals and patients with temporal lobe epilepsy (TLE). We studied functional activations during episodic and semantic memory task states and mapped spatial gradients of connectivity in the mesiotemporal lobe and neocortical networks. Moreover, we assessed whether gradient alterations are associated with performance on the memory tasks. The use of gradients allowed us to address whether networks subserving different aspects of declarative memory undergo a shared or selective reorganization in TLE and whether memory deficits in patients relate more strongly to mesiotemporal relative to neocortical reorganization.

Cortical Gradients in Semantic Cognition
Tirso Gonzalez-Alam, University of York, UK

We use a combination of univariate, connectivity and multivariate fMRI analyses across three samples (combined N > 250) to identify distinct pathways that capture the length of the principal intrinsic connectivity gradient from visual cortex to DMN. We then demonstrate a functional dissociation between these pathways in memory-guided decisions across two domains (semantic and spatial). The ends of these pathways correspond with previously-established functional dissociations in both visual cortex (between objects and scenes), and in default mode network (between semantic cognition and scene construction). Frontotemporal DMN regions are primarily engaged by semantic judgements and show stronger connectivity to object perception regions in lateral ventral occipital cortex, while medial temporal DMN regions are more strongly recruited during spatial judgements and show stronger connectivity to medial visual regions involved in processing scenes. We localise these pathways in the left and right hemispheres within a gradient space, focusing on the two components explaining the most variance in intrinsic connectivity.

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The semantic pathway is more heteromodal than the context pathway on Gradient 1, consistent with the observation that semantic cognition is more abstract than spatial cognition. This effect is stronger in the left hemisphere, in line with the lateralisation of semantic cognition. The spatial pathway is also more visual on Gradient 2, consistent with the privileged relationship between visual perception and spatial processing. The semantic pathway has lower spatial correlations with Gradient 2 in the left hemisphere, showing its inputs are more balanced across visual and auditory-motor networks. These analyses help to show how different variants of memory-based cognition can emerge from the intersection of the principal gradient with primary sensory-motor systems.

Tools for Multimodal, Multiscale Annotation of Brain Networks
Justine Hansen, Montreal Neurological Institute, McGill University, Canada

The development of advanced neuroimaging techniques has made it possible to annotate the brain in increasingly rich detail. In parallel, the open science movement has given researchers from diverse disciplines access to an unprecedented number of human brain maps. Integrating multimodal, multiscale human brain maps is necessary for broadening our understanding of brain structure and function. Here we introduce neuromaps, an open-access Python software toolbox for contextualizing human brain maps. Neuromaps currently features over 60 curated brain maps, including genomic, neuroreceptor, microstructural, electrophysiological, developmental, and functional ontologies. The toolbox implements functionalities for generating high-quality transformations between four standard neuroimaging coordinate systems, and can parcellate vertex- and voxel-level data according to a specified brain atlas. Robust quantitative assessment of map-to-map similarity is enabled via a suite of spatial autocorrelation-preserving null models, including permutation-based and generative models.

Neuromaps combines open-access data with transparent functionality for standardizing and comparing brain maps, providing a systematic workflow for comprehensive structural and functional annotation enrichment analysis of the human brain. Collectively, neuromaps represents a step towards creating systematized knowledge and rapid algorithmic decoding of the multimodal multiscale architecture of the brain.

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Intrinsic Timescales as a Unifying Organizational Principle of Neural Processing in Nonhuman Primates
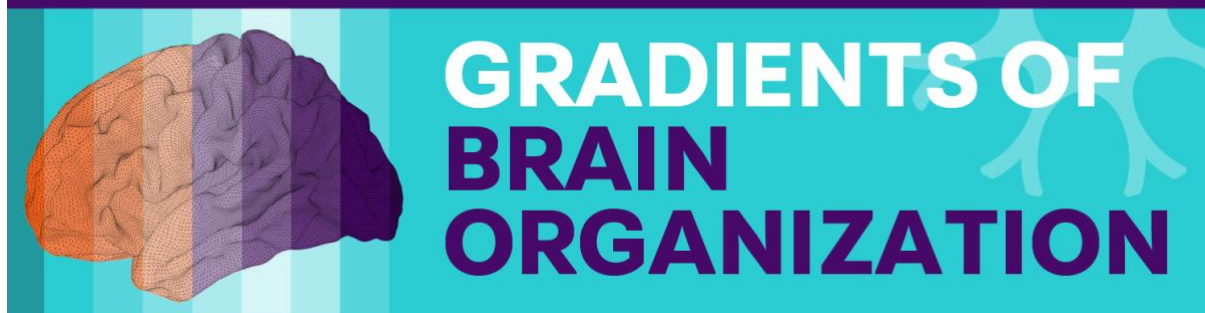
Ana M. G. Manea, University of Minnesota, USA

Hierarchical temporal dynamics are a fundamental computational property of the brain; however, there are no whole-brain, noninvasive investigations into timescales of neural processing in animal models. While traditionally investigated only in electrophysiology, recent advancements in functional magnetic resonance imaging (fMRI) make it possible to study hemodynamic timescales. We used the spatial resolution and sensitivity of ultra-high field (10.5 Tesla) fMRI to probe timescales across the whole macaque brain; hence moving investigations from single cells to macroscale dynamics. Timescales of baseline neuronal activity vary across the brain, from fast timescales in sensory areas, to slower timescales in association areas. In a group of nine nonhuman primate, we uncovered within-species consistency between neural timescales estimated from fMRI and electrophysiology. Despite efforts to understand the relationship between connectivity and neural timescales, the relationship to functional connectivity (FC) has not been elucidated yet since high-resolution fMRI data in nonhuman primates is scarce. We advance the field by examining the relationship between whole-brain FC and neural timescales topographies. Notably, we show that one facet of the high-dimensional FC architecture of the brain is closely related to temporal dynamics. The macroscale functional organization of the brain, as reflected by both temporal and spatial neural dynamics, is organized along gradual topographies at any level of description. Finally, investigating the macaque brain can bring an invaluable translational contribution. We demonstrate how gradients of functional connectivity and neural timescales can be used as a translational tool to uncover functional changes associated with the stages of addiction in nonhuman primates.

Why Cognitive Neuroscience Needs a State Space

Bronte Mckeown, Queen's University, Canada

Different situations pose different demands on an agent. For example, situations can vary in how much they require sustained attention or how much they rely on information from memory. As such, efficient behavior depends on accurately matching ongoing cognition and behavior to the specific set of situational demands. Building a mechanistic account of behaviour, therefore, requires us to understand how brain states underlying cognition 1) vary between situations and 2) how they change over time.

Although the neuroscientific community has developed many tools for parsing the landscape of brain activity into regions with similar functional behavior (i.e., parcellation), we currently lack an equivalent method for grouping together different brain states that emerge in different situations and over time. This talk will explain how a common space can be constructed using dimensions of variation in brain activity to examine the similarities and differences between brain states.This 'state space' allows us 1) to group situations based on the apparent similarities in the brain states and 2) empirically determine the different moments of brain activity that dynamically emerge over time. In this way, a common state space will provide an important method for understanding the neural mechanisms that allow humans to succeed in a wide range of different situations.

Organization of Laminar Thickness Covariance in the Human Cortex

Amin Saberi, Max Planck Institute for Human Cognitive and Brain Sciences and Forschungszentrum Jülich, Germany

The human neocortex consists of tangentially organized layers with unique cytoarchitectural properties. These layers show spatial variations in thickness and cytoarchitecture across the neocortex, which is thought to support brain function through enabling targeted corticocortical connections. In this study, leveraging maps of the six cortical layers in 3D human brain histology, we aimed to quantitatively characterize the systematic covariation of laminar structure in the cortex and its functional consequences. We identified a spatial pattern of changes in laminar thickness covariance from lateral frontal to posterior occipital regions, which differentiated the dominance of infra- versus supragranular layer thickness. Corresponding to the laminar regularities of cortical connections along cortical hierarchy, the infragranular-dominant pattern of laminar thickness was associated with higher hierarchical positions of regions, mapped based on resting-state effective connectivity in humans and tract-tracing of structural connections in macaques. The cortical maps of cortical hierarchy and laminar thickness variability were co-aligned with gradients of cortical microcircuitry. Moreover, we show that regions with comparable laminar thickness patterns correspond to inter-regional structural covariance, maturational coupling, and transcriptomic patterning, indicating developmental relevance. In sum, we characterize the association between organization of laminar thickness, processing hierarchy, and microcircuitry, anchored in ontogeny.
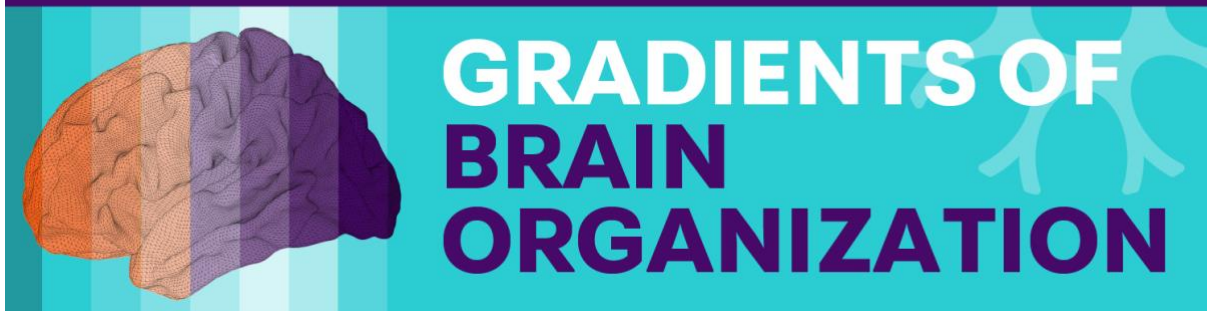
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Neural State Dynamics Along the Canonical Gradients of Functional Brain Organization Reflect Cognitive and Attentional Dynamics

Hayoung Song, University of Chicago, USA

Our mental states change constantly as we engage with the external world and our internal thoughts. In this study, we ask what neural states recur as we cycle through different mental states in diverse contexts. We investigate the shared underlying manifold of these neural states, how neural states transition from one state to another, and how these dynamics are linked to our cognitive and attentional states. We conducted functional magnetic resonance imaging as human participants performed attention tasks, watched comedy sitcom episodes and an educational documentary, and rested. Whole-brain dynamics traversed a common set of latent states that spanned canonical gradients of functional brain organization, with transient global desynchronization observed at state transitions. Neural state dynamics were synchronized across people during engaging movie watching and aligned to narrative event boundaries. Neural state dynamics reflected attention fluctuations such that different states indicated engaged attention in task and naturalistic contexts whereas a common state indicated attention lapses in both contexts. Together, these results demonstrate that traversals along large-scale gradients of human brain organization reflect cognitive and attentional dynamics. This study illustrates one way in which the brain flexibly gives rise to diverse experiences as activity travels between states in a shared manifold.

Gradients Go to the Movies: Macroscale Cortical Organization During Naturalistic Viewing

Tamara Vanderwal, University of British Columbia, Canada

Resting state gradients highlight a hierarchical organization of the brain, with apposition between heteromodal and primary sensory regions defining the first gradient. But how do functional connectivity (FC) gradients look when both heteromodal and unimodal brain regions are active and engaged? We hypothesized that applying diffusion embedding to FC data from movie-fMRI would reveal gradients with unique features, and that movie gradients might be more mathematically or geometrically "perfect" relative to resting state gradients. In this talk, I will show our recent findings on movie gradients in healthy adults, focusing on their topography and the movie gradient features we think will be most useful going forward. I will also show new results looking at age- and sex-based differences in movie gradients in a large sample of children, adolescents, and late adolescents.

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Friday, July 21 | 9 a.m. EDT   Jeanne Timmins Amphitheatre, The Neuro

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Overall, the talk aims to demonstrate that movie gradients provide increased granularity and a way to assess regions across modality-specific gradients that can reveal new information about functional brain organization in developmental and clinical populations.

Regional Cytoarchitecture Tracks Cortical Network Homogeneity and Heterogeneity

Yezhou Wang, McGill University, Montreal, Canada

Defining the functional units of the human cortex is a key goal of neuroscience. Recent studies have derived low-dimensional, continuous representations of cortical organization, also referred to as gradients, using cortex-wide decompositions of functional, microstructural, and structural connectivity features. The current work characterizes functional, microstructural, and structural gradient features within the probabilistic atlas of cortical cytoarchitecture, and assessed the uniqueness and redundancy of gradient profiles across cytoarchitecturally-defined cortical areas.

In this work, we studied 7 Tesla (7T) T1-weighted Magnetic Resonance Imaging (MRI), resting-state functional MRI, myelin-sensitive quantitative T1, and diffusion MRI of 10 unrelated healthy adults. Specifically, our work (i) took advantage of high-resolution 7T MRI to construct vertex-wise structural, microstructural, and functional connectomes, (ii) captured gradients profiles of brain regions through the integration of multimodal MRI and probabilistic atlas of cortical cytoarchitecture, (iii) assessed inter-parcel heterogeneity and homogeneity of multimodal features to quantify the uniqueness and redundancy of gradient fingerprints, and (iv) assessed intra-parcel heterogeneity between cortical vertices. To verify these findings, we repeated the main analyses on an independent dataset with 50 healthy adults.

Vertex-wise gradients of multimodal MRI data showed different spatial patterns across the cortex, indicating diverse hierarchies between vary modalities. By estimating cosine similarity between cortical regions, we found higher homogeneity in paralimbic regions and lower homogeneity in idiotypic i.e., sensory and motor cortices. To examine inter-parcel heterogeneity, we computed cosine distance between parcel-wise gradient profiles. We observed the highest heterogeneity in primary sensorimotor cortices, and lowest heterogeneity in paralimbic network ($p<0.05$, FDR corrected). Finally, we found that for most cortical parcels, vertices within a parcel are homogenous and show similar patterns among multimodal gradients. However, higher intra-parcel heterogeneity was found in heteromodal system ($p<0.05$, FDR corrected), while lower heterogeneity was found in idiotypic and paralimbic systems ($p<0.05$, FDR corrected). We repeated the main analysis on the validation dataset and found similar results.

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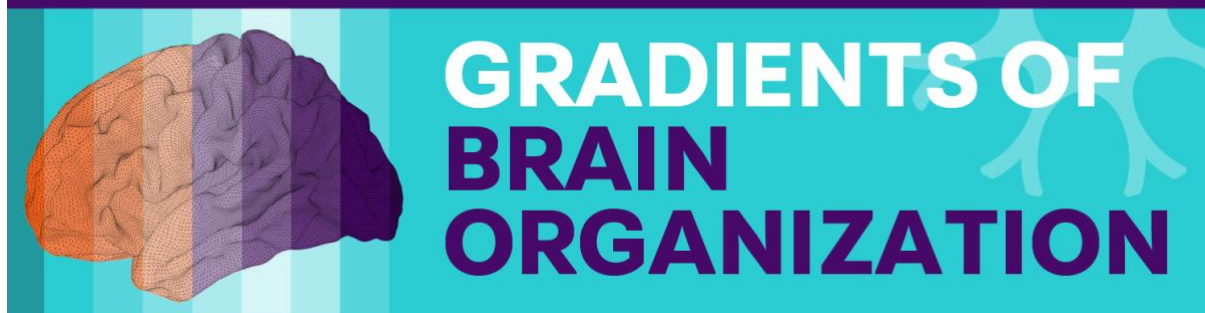
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Our findings point to a sensory-paralimbic differentiation of cortex-wide gradient fingerprints, where sensory/motor regions being more heterogenous compared to less distinctive paralimbic cortices. By reconciling local and global cortical features, our work may provide new insights into the neuroanatomical basis of specialized and integrative cortical functions.

Atypical Connectome Topography and Signal Flow in Temporal Lobe Epilepsy

Ke Xie, Multimodal Imaging and Connectome Analysis Laboratory, McConnell Brain Imaging Centre, Montreal Neurological Institute and Hospital, McGill University

Temporal lobe epilepsy (TLE), a common pharmaco-resistant epilepsy in adults, is typically related to hippocampal pathology. It is increasingly characterized as a system-level disorder with extensive network reorganization. Here, we combined connectome gradient and whole-brain effective connectivity analyses to investigate associations between imbalances of functional connectome hierarchy and intrinsic signal flow perturbations.

We studied 95 pharmaco-resistant unilateral TLE patients (43 males; mean±SD age = 31.2±10.6 years, 55 left-sided TLE) and 95 healthy individuals (45 males; 31.5±8.4 years) who were aggregated from three imaging sites (EpiC, MICA-MICs, and NKG). All participants underwent T1-weighted and resting-state fMRI (rs-fMRI) scans. We applied diffusion map embedding, a non-linear manifold learning technique, to cortex-wide functional connectomes derived from rs-fMRI data in each individual to identify connectome gradients. Surface-based linear models compared the principal gradient in TLE vs. controls using SurfStst, with age, sex, and site as covariates. Findings were corrected for multiple comparisons at a false discovery rate (FDR) < 0.05. We also summarized the surface-based results with a functional atlas of twelve networks. We further examined the association between TLE-related alterations in connectome gradients and intrinsic brain activity flow. Specifically, we modeled the whole-brain effective connectivity by applying regression dynamic causal modeling, a computationally efficient approach for inferring directed connectivity strength between regions, to the rs-fMRI data (360 regions). Here, node-wise OUT- and IN-degree were computed to quantify the amount of information a region sends to or receives from the rest of the brain, respectively. For the clusters exhibiting significant group gradient differences, we examined across-subject correlations between gradient and OUT-/IN-degree scores in TLE and control group separately.

The principal gradient (explaining 24% of connectivity variance) in both control and TLE groups were organized along a gradual axis from the unimodal to transmodal regions (i.e., the unimodal-transmodal gradient). Globally, the extremes of the unimodal-transmodal gradient were contracted in TLE relative to the control range, indexing functional dedifferentiation. Surface-wide comparisons revealed significant alterations in the bilateral temporal lobe, parahippocampus, and ventromedial prefrontal cortices in TLE (pFDR < 0.05). Stratifying the topography into functional communities identified lower gradient scores in the default mode network (DMN) but higher in the secondary visual network (VS2) and cingulo-opercular network (CON) (pFDR < 0.05). Leveraging regression dynamic modeling, TLE additionally showed lower OUT- and IN-degree scores in the abovementioned regions than controls (pFDR < 0.05), indicating less outward/inward signal flow. Moreover, both OUT- and IN-degree scores were significantly correlated with individual gradient scores across patients. That is, the less outward/inward signal flow, the lower the connectome hierarchy. In contrast, only a weaker, but significant association between gradient and IN-degree scores was found in healthy controls (r = 0.20, p = 0.024).

Leveraging multi-site MRI and multi-method analyses, we provide converging evidence for global-level functional imbalances in patients with pharmaco-resistant TLE. These findings demonstrated alterations in the principal functional gradient and underlying neural mechanisms.

Structure-Function Plasticity Coupling for Improved Perceptual Decisions
Liz Yuanxi Lee, University of Cambridge, UK

Introduction: Experience and training are known to boost our skills and alter the brain's structure and function. Yet, our understanding of how structural and functional brain plasticity mechanisms interact to support learning for perceptual decisions remains limited. Here, we employ multimodal brain imaging to investigate the links between microstructural (i.e. myelination) and functional (i.e. connectivity) mechanisms that support perceptual decisions. We investigate interactions between large-scale spatial trends (i.e., gradients) to assess systematic changes in structure and function across brain networks involved in learning (Royer et al., 2022).

Methods: Twenty-two participants were trained on a signal-in-noise (SN) task that involves discriminating radial vs. concentric Glass patterns (Glass 1969). Participants completed six experimental sessions over nine days: three brain imaging sessions (day 1: baseline, day 5: pre-training, day 9: post-training) and three consecutive behavioural training sessions (day 6-8). For each brain imaging session (Siemens 3T Prisma), we collected: a) T1-weighted (T1w), proton density-weighted (PDw) and magnetization transfer saturation (MTsat) data using FLASH multi-parameter mapping (MPM), and b) resting state fMRI (rs-fMRI) using Echo-planar imagining.

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We computed microstructural and functional gradients using the hMRI toolbox (Tabelow et al., 2019) and the micapipe toolbox (Cruces et al., 2022), and structure-function coupling using microstructural profiling and functional connectivity covariance (Baum et al., 2020). Learning-dependent changes were computed by subtracting post- from pre-training data normalized to baseline. We used gene expression data from Allen Human Brain Atlas (AHBA) (Hawrylycz et al. 2012) with abagen toolbox (Markello et al. 2021) to predict learning-dependent imaging changes (e.g., structure-function coupling, microstructural gradient) with partial least squares regression (PLSr). Using a permutation test for significant PLSr components and bootstrapping for significant genes, we conducted enrichment test with FUMA GWAS (Watanabe et al., 2017). We computed within-network and between-network dispersion of microstructural and functional gradients (Bethlehem et al., 2020) within frontoparietal (cognitive control) and default mode networks (Yeo et al., 2011).

Results: Enrichment test for gene expression showed that frontoparietal (cognitive control, known to be involved in the SN task) and default mode network (Yeo. et al., 2011) can predict learning-dependent changes in microstructural gradient changes and coupling changes. Learning-dependent changes in dispersion of principal functional gradients in cognitive control network correlated significantly with learning rate ($r = .564$, $p = .023$). Between-network dispersion (cognitive control network and default mode network) correlated significantly with behavioural performance improvement ($r = .556$, $p = .020$). There were no significant correlations between changes in microstructure gradients and learning rate, suggesting that training alters functional rather than structural connectivity for improved perceptual decisions. Relating changes in structure-function coupling to learning rate showed significant negative correlations (cognitive control, $r = -0.680$, $p = .004$; default mode network, $r = -0.613$, $p = .012$), suggesting that faster learning rate relates to stronger structural-functional connectivity decoupling.

Conclusions: We find that learning-dependent changes in functional connectivity dispersion and structure-function coupling in decision-related and default mode networks relate to learning rate in perceptual decision tasks. These results suggest that structure-function plasticity coupling is key for improving perceptual decisions through training.

Large-scale Biophysical Models and Neuronal Dynamics
Shaoshi Zhang, National University of Singapore, Singapore

A balanced excitation-inhibition ratio (E/I ratio) is critical for normal brain function. In this talk, I will present an approach to non-invasively estimate whole-cortex E/I ratio by fitting a large-scale biophysically plausible circuit model to resting-state fMRI data. We apply this approach to study E/I ratio changes during development. We find that E/I ratio is lower for older children compared with young children in a North American Cohort. E/I ratio reduction rate exhibits a spatial gradient with faster decline in sensory-motor networks than association networks. Importantly, among children with the same chronological age, lower E/I ratio is more strongly associated with better cognition in the association networks than sensory-motor networks. This result was replicated in an independent Asian cohort. These results suggest that the

estimated E/I ratio indexes biological maturity beyond chronological age. Overall, this approach opens the door to the study of cortex-wide E/I ratio changes across the lifespan and in neuropsychiatric disorders.

POSTER ABSTRACTS

No Rest for the Wicked: Gradients Derived Solely from Time-Locked, Stimulus-Driven Connectivity Patterns
Ahmad Samara, University of British Columbia, British Columbia, Canada

We recently showed that functional connectivity (FC) gradients during movie-watching are hierarchical and modality-specific: the top three movie gradients delineate separate axes anchored in sensorimotor, visual, and auditory/language areas (Samara 2023). BOLD-signal dynamics during naturalistic processing likely reflect the sum of multiple sources of variability including stimulus-induced signal, intrinsic neural signal (i.e., spontaneous fluctuations) and multiple sources of non-neuronal variability (e.g., physiological noise) (Nastase 2019). To characterize large-scale cortical organization based only on time-locked, stimulus-driven connectivity patterns, we computed gradients using intersubject functional connectivity (ISFC) matrices (Simony 2016), and examined their topography, test-retest reliability, and correlation with behavioural scores.

Data are from 95 subjects (58 females, mean age=29.5±3.3 years) from the Human Connectome Project 7T release, with four 15-minute movie-watching fMRI runs and a wide range of behavioural measures. Movie runs were concatenated and vertex-wise functional timeseries were averaged based on their assignment to the Schaefer-1000 parcellation. ISFC was computed as the parcel-by-parcel matrix of correlation values between one subject's parcelwise time-course and the group-averaged time-course for all other parcels. The resulting asymmetric matrix was replaced by the average of the two off-diagonal values. Individual- and group-level ISFC matrices were decomposed using diffusion embedding (Margulies 2016; vos de Wael 2020), creating ISFC-based gradients. Reliability was assessed using intraclass correlation (ICC) of gradients computed across two scanning sessions. Principal component analysis was applied to behavioural measures in cognitive, emotion, and motor domains, yielding a summary component for each subject for each behavioural domain, and correlations were computed between ISFC gradient scores and those summary components.

Gradients from ISFC matrices explained a comparable amount of variance to those from FC, and were also each anchored by a distinct perceptual modality. Homologous FC and ISFC

gradients were topographically similar, with the auditory/language gradient demonstrating the highest correlation (r=0.71, FC to ISFC). ISFC gradients 1-4 also had high test-retest reliability (mean ICC=0.81; FC gradients: mean ICC=0.83). Correlations with behaviour were even weaker for ISFC gradients compared to FC gradients (e.g., principal gradient-cognitive mean r=0.05 for ISFC vs. 0.14 for FC).

The preserved gradient topography when using ISFC matrices suggests that cortical organization during movie-watching is dominated by shared, stimulus-evoked connectivity patterns. The auditory/language gradient–a unique movie gradient that is absent during rest–shows the highest similarity when using only synchronized stimulus-driven connectivity with "unfiltered" within-subject FC. The weaker brain-behaviour correlations with ISFC may be due to the lack of synchronized activity during movie-watching in prefrontal regions, and/or aspects of idiosyncratic stimulus-related processing that are not time-locked but may play an important role in individual differences. Altogether, ISFC gradients appear to filter out important but non-time-locked information about brain connectivity that exists within regular FC movie-watching matrices. They provide a useful framework to help interpret and understand results from FC-based movie-watching studies but likely provide a somewhat impoverished reflection of connectivity relative to standard FC movie gradients.

Geometric Constraints on the Functional Organisation of the Infant Cerebral Cortex
Alexander Holmes, Monash University, Australia

Numerous studies analysing resting-state fMRI connectivity via low-dimensional functional gradients have shown that the adult cerebral cortex is arranged along a unimodal-to-transmodal axis reflecting the classical sensory-fugal processing hierarchy. Neural field theory posits that this functional organisation likely arises from the anatomical organisation and geometry of the cortex. Specifically, the coupling of cortical geometry with simple distance-dependent connectivity, where coupling strength between cortical locations declines with their physical separation via an exponential distance rule (EDR), represents a powerful and fundamental structural constraint on macroscale brain dynamics. Accordingly, neural field theory predicts a direct correspondence between the geometric and functional modes of the cortex. However, the dominant geometric mode follows a simple anterior-to-posterior pattern that deviates from the classical sensory-fugal hierarchy observed in functional gradients.

One possibility is that empirical connections beyond a simple EDR drive this divergence, suggesting long-range coupling may be required for hierarchical functional modes to emerge. Under this hypothesis, the convergence between geometric and functional modes of the cortex should be greater in early development before the maturation of such long-range connections.

Here, we test this prediction by examining the correspondence between geometric and functional modes of the cerebral cortex during infancy.

Using MRI data from 282 individuals in the UNC/UMN Baby Connectome Project, aged 1-60 months, we computed resting-state functional connectivity (FC) by estimating pair-wise correlations between vertex-level timeseries extracted from 10,686 cortical surface vertices. We then calculated low-dimensional connectivity manifolds from individual FC matrices via diffusion map embedding. Alongside individual-specific manifolds, we produced group-level manifolds from averaged FC matrices across key developmental age bands at 0-2, 3-5, 6-11, 12-17, 18-35, and 36-60 months. Geometric modes were obtained at each age band by deriving the eigenmodes of the Laplace-Beltrami operator applied to age-specific cortical surface mesh templates from the UNC 4D Infant Cortical Surface Atlas.

In contrast to the sensory-fugal gradient observed in adults, the dominant infant functional gradient followed an anterior-to-posterior pattern across all age bands. This anterior-to-posterior gradient was consistently highly correlated with the first non-constant geometric mode (0-2 months: r=0.85; 3-5 months: r=0.96; 6-11 months: r=0.94; 12-17 months: r=0.90; 18-35 months: r=0.90; 36-60 months: r=0.82). The proportion of variance in FC explained by the anterior-to-posterior gradient appeared to peak in earlier stages of infancy, representing 32.24% of variance at 0-2 months, 42.92% at 3-5 months, 43.55% at 6-11 months, 38.72% at 12-17 months, 29.94% at 18-35 months, and 32.89% at 36-60 months.

The dominant infant functional gradient demonstrates an anterior-to-posterior topographical organisation, which differs from the expected sensory-fugal pattern found in adults and adolescents but coincides with the dominant geometric mode. This finding suggests that there is a direct correspondence between modes of geometry and function in infancy, as predicted by neural field theory, and that their divergence with age may be a consequence of the maturation of long-range axonal fibres.

In Vivo Mapping of Pharmacological Functional Reorganisation onto the Brain's Neurotransmitter Landscape
Andrea Luppi, Montreal Neurological Institute, McGill University

Psychoactive compounds induce profound but reversible alterations of brain function. In combination with non-invasive brain imaging techniques such as functional MRI, acute pharmacological interventions have emerged as a prominent tool for causal investigation of the relationship between brain and cognitive function (Wandschneider and Koepp, 2016, Neuroimage Clinical). To understand how pharmacological interventions can exert their powerful effects on brain function, we need to understand how they engage the brain's rich neurotransmitter landscape.

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Here, we bridge microscale molecular chemoarchitecture and pharmacologically-induced macroscale functional reorganisation, by mapping the regional distribution of 19 neurotransmitters obtained from Positron Emission Tomography, onto the regional changes in functional MRI connectivity induced by 10 potent psychoactive pharmacological agents, covering the range from anaesthetics to psychedelics.

To map the functional chemoarchitecture of the human brain, we leveraged two unique datasets: (i) a recently assembled collection of in vivo PET maps of regional receptor expression from 19 different receptors, providing the most detailed information about neurotransmitters and their spatial distribution available to date (Hansen et al., 2022, Nature Neuroscience); and (ii) resting-state fMRI data acquired under the effects of the general anaesthetics propofol and sevoflurane; the cognitive enhancers modafinil and methylphenidate; ketamine, acting as both atypical psychedelic (at sub-anaesthetic doses) and as dissociative anaesthetic; and the serotonergic psychedelics LSD, psilocybin, DMT, ayahuasca, and MDMA – representing a total of 382 sessions of pharmacological-MRI.

We employed a multivariate association technique, Partial Least Squares analysis, to identify multivariate patterns of maximum covariance between drug-induced effects on functional connectivity, and the cortical distributions of neurotransmitter expression. Significance was assessed against autocorrelation-preserving spin-based null models. We also compared regional susceptibility to pharmacologically-induced functional alterations, and regional susceptibility to disease-associated cortical thickness abnormalities from 21,000 patients made available by the Enhancing Neuro Imaging Genetics Through Meta Analysis (ENIGMA) consortium (Larivière et al., 2021, Nature Methods; Thompson et al., 2020, Translational Psychiatry).

Our PLS analysis indicated the presence of two statistically significant latent variables relating pharmacologically-induced functional reorganisation to neurotransmitter profiles, together accounting for nearly 85% of covariance. Our results further reveal that psychoactive drugs exert their effects on brain function by engaging multiple neurotransmitter systems. We found that the effects of mind-altering drugs are topographically organised along multiple hierarchical gradients of brain function, anatomy, and neurobiology. Finally, we discovered that regional co-susceptibility to pharmacological perturbations recapitulates co-susceptibility to disorder-induced structural perturbations from the ENIGMA consortium.

In conclusion, by relating microscale molecular chemoarchitecture and drug-induced macroscale functional reorganisation, our results provide a computational framework to bridge molecular mechanisms and their effects on cognition, via their influence on the brain's functional architecture.

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Sex Differences in Functional Cortical Organization Reflect Differences in Network Topology rather than Brain Geometry

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Although brain size shows robust sex differences, it is unclear whether it differentially shapes functional cortical organization between sexes through altered cortical geometry. Brain size is a major scaling factor unfolding along the sensory-association axis across evolution and development (Buckner & Krienen, 2013; Reardon et al., 2018). Functional and microstructural hierarchical differentiation also display patterns of short- and long-range connections across the cortical mantle, respectively clustered in sensorimotor and association regions (Wang et al., 2023).

Concurrently, females show stronger intrinsic functional connectivity (FC) in the default-mode network (DMN) and males between sensorimotor regions (Ritchie et al., 2018). Given that brain size seemingly explains some sex-specific variance in FC (Zhang et al., 2018) whilst cortical geometry appears to constrain brain-wide functional dynamics (Pang et al., 2023), we investigated whether sex differences in functional organization could be explained by differences in brain size, structure, and geometry.

In the Human Connectome Project dataset (N=1000, 28.73±3.71y, 536F), we probed structural and geometric properties potentially constraining functional organization using diffusion map embedding to dimensionally reduce FC to the sensory-association axis of functional organization. With correlations and linear mixed effects models (LMEMs), we tested effects of brain size, mean geodesic distance, and microstructural profile covariance (MPC) on functional organization. Then, we used LMEMs to identify sex differences in functional organization, network dispersion, and FC strength. The Chi-square test of independence probed sex differences in connectivity profiles (i.e., odds of areas constituting top 10% connections per seed region). Finally, correlation analyses determined the extent to which sex differences in MPC and mean geodesic distance may explain sex differences in functional organization. LMEMs included sex, age, and brain size as covariates, and controlled for random nested effects of family relatedness and twin status, and whole-brain results underwent false discovery rate correction. In correlation and network dispersion analyses, spin permutation testing (1000 permutations) controlled for spatial autocorrelation.

Functional organization showed negligeable effects of brain size, but strong associations with mean geodesic distance (r=0.76, pspin=.002) and mild associations with MPC (r=0.23, pspin=.026). Sex differences in functional organization were distributed across functional networks –prevailing in the DMN, frontoparietal, and ventral attention (VA) networks– and

were mildly associated with sex differences in connectivity profiles (r=.17, pspin=.005), but not in FC strength. Males showed greater dispersion within the DMN (t=2.65, pspin<.001) and VA (t=2.94, pspin<.001), whilst no sex difference in between-network dispersion survived Bonferroni correction. Sex differences in MPC and mean geodesic distance were not associated with differences in functional organization, although we observed sex differences in connectivity profiles as a function of mean geodesic distance.

Sex differences in functional brain organization do not appear to be explained by differences in brain size, structure, or geometry, although microstructure and mean geodesic distance may somewhat constrain functional organization. Instead, sex differences along the sensory-association axis are related to differences in connectivity profiles and within-network dispersion, in particular in the DMN and VA. Future work should explore the biological, cognitive, and environmental factors potentially driving system-level sex differences in network topology.

Reduced Differentiation of Intrinsic Neural Fluctuation Speed Under the Effects of Psilocybin
Brian Winston, Johns Hopkins University, Maryland, USA

Over a decade of multimodal neuroimaging research has revealed a gradient of regions in the human brain that integrate information from shorter (hundreds of milliseconds-long) to longer (minutes-long) timescales. Using electrocorticography (ECoG) and functional magnetic resonance imaging (fMRI) methods, respectively, Honey et. al (2012) and Stephens et. al (2013) demonstrated that this gradient of "temporal receptive windows" (TRWs) is subserved by a corresponding gradient of intrinsic speed of neural fluctuations. Regions with longer TRWs exhibit higher amplitude of low frequency signals (ALF) than regions with shorter TRWs. This gradient, which runs along the superior temporal gyrus (STG) from primary auditory cortex (A1) through the temporo-parietal junction to angular gyrus, appears not only while subjects observe naturalistic stimuli (e.g. audiovisual narratives or music that contains information across multiple timescales) but also at rest (Honey et. al 2012, Raut et. al 2020, Baria et. al, 2013).

The 5-HT2A agonists psilocybin and LSD have been shown to flatten the brain's functional gradient differentiating unimodal from transmodal cortex (Girn et. al, 2022); however, whether psilocybin alters the ALF gradient is unknown. Using a repeated measures, placebo-controlled design, we investigated the acute effects of 10mg/70kg of the 5-HT2A agonist psilocybin on the speed of neural dynamics across the cortex during both resting state and music listening fMRI sessions. We first successfully reproduced the ALF gradient along the STG during both resting state and music listening in the placebo condition. To evaluate a potential change in the gradient, we selected regions of interest in A1 and angular gyrus and ran a drug x ROI ANOVA. In the resting state condition, the ANOVA revealed a significant interaction of drug x

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ROI such that ALF was increased in A1 and reduced in angular gyrus under the effects of psilocybin, representing a flattening of the ALF gradient. We observed no such change in the music-listening condition. We plan to interrogate all of these data further.

Predicting early-stage Parkinson's Disease using Striato-Cortical Gradients
Dimuthu Hemachandra, School of Biomedical Engineering, University of Western Ontario, London, Canada & Robarts Research Institute, University of Western Ontario, London, Canada

Parkinson's disease (PD) is a highly complex neurodegenerative disorder that has no objective diagnostic tests, cures, or disease-modifying therapies. The lack of diagnostic measures hampers discovery of disease-modifying therapies and makes current PD management inefficient and imprecise. Traditional brain imaging studies have used hard parcellations to analyze discrete brain regions, overlooking the smooth spatial changes within connectivity patterns. To address this limitation, connectomic mapping (Coifman and Lafon 2006) techniques incorporating gradients have gained interest. Gradients capture continuous transitions in brain connectivity, offering a nuanced understanding of neural organization. This approach is particularly valuable in studying striato-cortical connectivity in PD and detecting alterations associated with disease progression. This study emphasizes the importance of capturing smooth spatial changes beyond traditional parcellations and highlights the efficacy of diffusion embedding. To overcome challenges in subject-wise comparisons, a novel approach utilizing Principal Component Analysis (PCA) as secondary dimensionality reduction is proposed. Preliminary results show diagnostic capabilities in detecting early-stage PD.

3 Tesla T1-weighted and diffusion weighted MRI data of early-stage (< 1year into the disease with an average of 6 months) 91 PD patients and 52 health controls were obtained from the Parkinson's Progression Marker Initiative(Marek et al. 2011). Structural connectivity matrices were obtained between striatal voxels and cortical regions of interest (ROIs, N=1000 as defined by the Schaefer atlas) after automatic segmentation of the T1w image using FreeSurfer. Diffusion embedding (Coifman and Lafon 2006) was applied for dimension reduction into so-called 'gradients'. The three striatal gradients (G1-3) explaining most of the variance were selected and projected back to striatum for visualization (Figure 1). We aimed to assess the effectiveness of the subject-specific gradients in distinguishing PD patients from healthy subjects. Principal Component Analysis (PCA) was applied to further reduce the dimensionality of each gradient. Group comparisons were performed using a two-tailed t-test. Additionally, a machine learning approach using a Random Forest classifier was employed, incorporating PCA components from G1 and G2, age, and sex as features (Figure 2).

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The first PCA component (G1_PCA1) exhibited significant differences between healthy subjects and PD patients at baseline (p < 0.008; Figure 3). A random forest classifier achieved 80% diagnostic accuracy, with sensitivity of 76% and specificity of 68% (Figure 4).

In this study, we investigated using low dimensional embeddings of striato-cortical connectivity to detect early-stage PD. The results showed significant differences between healthy subjects and PD patients, particularly with the G1 gradient, indicating its potential as a discriminatory feature. These findings highlight the potential of gradients as biomarkers for early-stage PD classification and severity assessment, while providing insights into striato-cortical connectivity changes in PD.

Linking Structural and Functional Imaging Modalities to Characterize Atypical Face Processing in Autism

Dorothea Floris, University of Zurich, Germany

Atypical emotional and face processing is among the core social difficulties of individuals with autism. However, pinpointing neural underpinnings of atypical face processing in autism has yielded inconsistent results across different imaging modalities. Most analyses have been confined to separate modalities and linking them has so far been a methodological and statistical challenge. By cutting across single-modality analyses, and integrating different imaging modalities that have been associated with atypical face processing previously, we aim to increase sensitivity in detecting underlying and shared mechanisms of face processing in autism. To this end, we leveraged the large-scale EU-AIMS Longitudinal European Autism Project (LEAP) dataset which has a rich battery of different structural and functional imaging modalities available. Using Linked Independent Component Analysis (LICA) we combined different structural and functional modalities that relate to face processing and integrated these findings with clinical information.

We included 101 individuals with autism and 101 typically developing individuals, aged between 6 and 30 years from the LEAP dataset. This sample size reflects the intersection of available data across the four imaging modalities that were integrated: a) neuroanatomy (voxel-based morphometry to derive grey matter volume within the fusiform gyrus), b) intrinsic brain activity (using resting-state fMRI we derived functional connectivity gradients within the fusiform gyrus based on connectopic mapping (Haak et al., 2017)), c) task fMRI during emotional face matching task (Hariri et al. 2002, contrast maps reflecting brain areas with higher sensitivity for emotional faces compared to shapes and confined these to the fusiform gyrus) and d) EEG-based event-related potential (ERP at P7/P8) timeseries in response to a facial stimuli paradigm. LICA (Groves et al. 2011, Llera et al., 2019) was used to simultaneously factorize all subjects' data into 50 independent components (ICs) of spatial variations. A Generalized Linear Model was used to examine case-control differences and univariate brain-behaviour associations while regressing out the effects of age, sex, and scanning site. Next, Canonical Correlation Analysis (CCA) (Winkler et al., 2020) was performed to quantify the aggregated effects between multi-modal ICs and subscales related to social functioning of ADI, ADOS, Social Responsiveness Scale, and the three Vineland

subscales. The statistical significance of each pair of canonical variates was determined by permutation testing (10,000 times).

Among the 12 multimodal independent components, one (IC45) showed a significant group difference with autistic individuals having lower contributions compared to neurotypical individuals (t=3.2, p=0.001, pFDR=0.02). This component was mostly driven by the right hemisphere (77.2%) and by functional modalities (EEG R [45.2%], task-fMRI R [25.7%], task-fMRI L [19.9%], rs-fMRI R [6.0%]). Applying multivariate CCA revealed a significant association between the multimodal ICs and the set of social-cognitive features (r=0.64, permutation p=0.009).

We successfully merged data across four different neuroimaging modalities to characterize a multimodal neurophenotype of autism in a key region (FFG) related to face processing and social functioning.Multimodal aspects related to face processing can explain inter-individual variance in social functioning and daily living skills in autistic individuals.

Transdiagnostic Mapping of Striatal Connectivity and Behavior-Circuit Modeling in Autism and ADHD

Han Byul Cho, Center for Neuroscience Imaging Research, Institute for Basic Science, Suwon, Republic of Korea

ASD and ADHD are developmental conditions that often co-occur in the same individual. Given that some of their symptoms are related to altered cognitive flexibility and reduced motor persistence, the striatum - a core structure for goal-directed action selection, motor execution and habituation - has been hypothesized as one of the common pathological substrates. Indeed, converging evidence indicates an abnormal corticostriatal circuit in both ASD and ADHD, particularly between the striatum and ventromedial/orbito-frontal (vmPFC/OFC) as well as the premotor cortex. However, how shared striatal anomalies could lead to seemingly distinct behavioral symptoms remains poorly understood. Here, we fill this gap through i) a fMRI connectome gradient mapping of the striatum from ASD and ADHD groups and ii) imaging-informed computational modeling of the corticostriatal circuit.

We leveraged two open imaging datasets (ABIDE-I and ADHD200) and targeted 46 ASD, 52 ADHD and matched 99 neurotypical (NT) individuals. In these samples, we constructed two connectopic maps of the striatum using nonlinear dimensionality reduction. Previously, the 1st striatal connectopic map (CMAP) has been associated to goal-directed behaviors, while the 2nd CMAP to dopaminergic transporter availability. We performed MANOVA to identify group differences in these CMAPs. We then also estimated seed-based connectivity between frontal and striatal regions showing the significant group differences. To test predictability of neuroimaging findings for symptom severity, we built a connectome predictive model using a simple linear regression (5-fold cv). Next, we implemented a striatal circuit model based on a Bayesian brain theory, which infers a next action to maximize the reward, and trained it for a reversal choice task, an established reinforcement learning task. In doing so, we adopted striatal connectivity values from each individual to perturb the normative circuit model to mimic the pathogenicity of ASD and ADHD, and examined the flexibility and inverted persistence of task performance.

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MANOVA of the striatal CMAP showed two clusters with significant group differences. Both clusters revealed decreased striatal connectivity in the frontal lobe, specifically decreased FC between the putamen and vmPFC/dmPFC (value/goal-directed systems) was observed in ASD, while decreased FC between the caudate and premotor cortex (motor-habit systems) characterized ADHD relative to NT. The predictive model, trained by the striatal connectivity values from these two clusters, demonstrated significant predictability to ASD symptoms severity in ASD total score and social interaction. The neuroimaging-informed computational model provided circuit-level mechanistic explanations for the behavioral symptoms. In the reversal task, both ASD and ADHD groups showed decreased task flexibility relative to controls, whereas the ADHD group further revealed decreased persistence in the task, indicating an abnormally increased variance.

While both ASD and ADHD commonly showed atypical striatal connectivity, distinct patterns for each condition were identified. On the one hand, ASD showed altered striatal connections in the anterior frontal regions, usually associated with value and goal-directed systems, possibly leading to flexibility deficits. On the other, the ADHD group showed altered connections mainly in the motor area, which may result in reduced persistence. Our study demonstrated a potential of neuroimaging-informed circuit modeling in computational psychiatry research.

Age-Dependent Cortical Gradients Along the Anatomical Axes of the Brain in Time-Series Features of MEG Resting-State Recordings

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A long-standing goal in systems neuroscience is to understand the relationship between the structural anatomy and the function of the brain in order to gain insight into its organizing principles. Gradients have been used in the literature to describe the topographic organization of features throughout the human cortex with the advantage of capturing continuous changes globally across the cortex. In detail, significant spatial gradients, predominantly in the posterior-anterior direction, have been reported for various structural measures of the brain, such as cytoarchitecture, myelination, and cortical thickness, as well as brain activity features, including functional connectivity and peak frequency.

To extend the current understanding of cortical gradients beyond the measures already studied, we aim to investigate the cortical distribution of other brain activity-related time-series features that may provide additional information. Therefore, in this study, we utilized the extensive highly comparative time-series analysis toolbox (hctsa) and computed in total 5737 time-series features on 5 min resting-state, source-reconstructed MEG recordings of 350 participants (age: 18-88) obtained from the CamCAN data set. In particular, we explored whether these features show gradients along the anatomical axes of the brain using linear mixed effect model analyses.
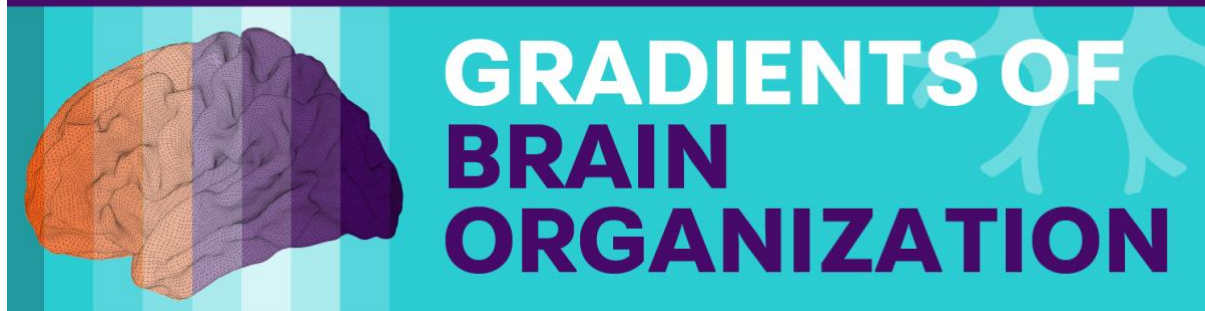
GRADIENTS OF BRAIN ORGANIZATION

We found that many features demonstrate highly significant gradients along the brain's axes. Of these, the most significant gradients are present along the posterior-anterior brain axis. These include, for instance, features related to the Fourier spectrum but additionally autocorrelation, forecasting, and scaling measures. Strong gradients can be also demonstrated along the superior-inferior axis, which particularly cover features associated with modeling of future time-series values. In addition, we detected significant features such as entropy and non-linear correlation measures along the brain's medial-temporal axis. Interestingly, gradients of features from the hctsa toolbox showed stronger gradients compared to power in canonical frequency bands. When ranking the features with the most significant gradients along the posterior-anterior axis, alpha spectral power is ranked 12th and delta spectral power is only ranked 181th, even though they show the strongest posterior-anterior gradients out of the canonical frequency bands. Indeed, features show significant gradients even when spectral power information from the canonical frequency bands (delta, theta, alpha, beta, gamma) were removed via linear regression along the respective axis. Lastly, we were able to show that the topography of particular feature gradients changes with age along all three anatomical axes of the brain. Our results demonstrate that comprehensive time-series feature phenotyping reveals information about the spatial distribution of brain dynamics over and above what is captured in canonical frequency bands. Our work represents the first steps in the direction of uncovering multivariate electrophysiological functional fingerprints of hierarchically organized anatomical brain structures.

Healthy Aging Alters the Content of Neurophysiological Fingerprints but not their Accuracy

Jason da Silva Castanheira, Montreal Neurological Institute, McGill University, Canada

Brain-fingerprinting is a tool to advance the neuroscience of inter-individual diversity in health and disease. We used magnetoencephalography (MEG) cortical imaging to study how the features of brain-fingerprints evolve in healthy ageing. We derived the neurophysiological brain-fingerprints of 606 individuals from 18 to 89 years of age from up to eight minutes of task-free MEG recordings. We found that individuals can be differentiated from each other from their brain activity with 90% accuracy. Remarkably, individuals remain differentiable even when using considerably shorter data segments of 30 seconds. We found that the most salient neurophysiological features for inter-individual differentiation can also distinguish individuals' performance in fluid intelligence tests. The accuracy of inter-individual differentiation is weakly related to age (r2 = 0.046, p < .001) with a 92% accuracy between young adults (18-45 years old) and 93% between older adults (65-89 years old). However, we noted that the most differentiable neurophysiological features change with age, and follow a superior-to-inferior anatomical gradient along the cortex. Older adults are better differentiated from the brain activity in their dorsal cortices; younger adults are better differentiated from the brain activity of ventral cortical regions. We also demonstrate that the cortical regions where the brain-fingerprint features change with age are also key to decode the general cognitive abilities of participants.

How the brain-fingerprint changes with age overlaps with the unimodal-to-transmodal gradient of the cortex' functional hierarchy, and the serotonin and norepinephrine systems of the cortex. Overall, our study provides evidence that neurophysiological brain-fingerprinting is robust across the wide age range of adulthood, yet the most salient features for individual differentiation evolve with age. We discuss the importance of considering underlying differences in the contents of brain-fingerprints when differentiating individuals across varying demographic groups.

Abnormal higher-order network interactions in Parkinson's disease visual hallucinations

Joshua B. Tan, University of Sydney, Australia

Visual hallucinations in Parkinson's disease can be viewed from a systems-level perspective, whereby abnormal communication between brain networks responsible for perception predisposes a person to hallucinate. Specifically, alterations between higher-order and primary sensory networks have been implicated in the pathophysiology of visual hallucinations in Parkinson's disease.

Dimensionality reduction techniques offer a novel means for simplifying the interpretation of multidimensional brain imaging data, identifying patterns in the data that are driven by both within- and between- network changes. Here, we applied two complementary non-linear dimensionality reduction techniques – diffusion-map embedding and t-distributed Stochastic Neighbour Embedding (t-SNE) – to resting state fMRI data to better understand the altered functional hierarchy associated with susceptibility to visual hallucinations in 77 people with Parkinson's disease (31 with hallucinations; 46 without hallucinations) and 19 age-matched healthy controls. In patients with visual hallucinations, we found compression of the unimodal-heteromodal gradient – consistent with increased functional integration between sensory and higher order networks. This was mirrored in a traditional functional connectivity analysis, which showed increased connectivity between the visual and default-mode networks in the hallucinating group. Together, these results suggest a route by which higher-order regions may have excessive influence over earlier sensory processes, consistent with models of hallucinations across disorders. By contrast, the t-SNE analysis identified distinct alterations in prefrontal regions that were not apparent from direct comparisons of functional connectivity matrices. The results confirms abnormal brain organisation associated with the hallucinating phenotype in Parkinson's disease and highlight the utility of applying convergent dimensionality reduction techniques to investigate complex clinical symptoms.

In addition, the patterns we describe in Parkinson's disease converge with those seen in other conditions, suggesting that reduced hierarchical differentiation across sensory-perceptual systems may be a common transdiagnostic vulnerability in neuropsychiatric disorders with perceptual disturbances.
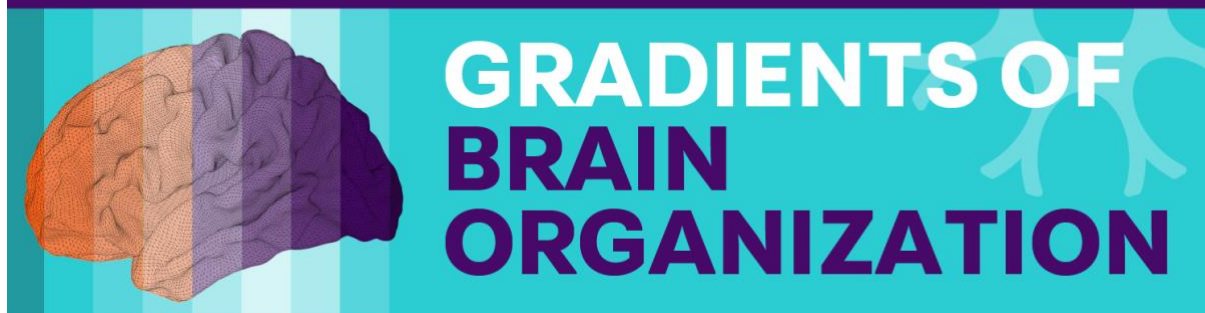
Association between brain network stratification and cognition in schizophrenia spectrum disorders (SSD)

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Schizophrenia Spectrum Disorders (SSD) have been associated with dysconnectivity in "lower-order" (e.g., visual, auditory) and "higher-order" (e.g., default-mode and frontoparietal) cortical networks (Dong et al., 2018; Oliver et al, 2021). Previous studies used diffusion map embedding (Margulies et al., 2016) to characterize different levels of cortical and subcortical hierarchy by gradient principal components in SSD (Dong et al., 2020; Wang et al., 2020). These studies found SSD showed less dissociation between the lower- and the higher-order networks which was captured by compression of the first gradient. This gradient was correlated with the severity of clinical symptoms (Dong et al., 2020; Wang et al., 2020) and processing speed (Wang et al., 2020). However, as psychiatric disorders are strongly related to both neurocognitive (i.e., non-social) and social cognitive deficits, little is known about how such cortical and subcortical hierarchy is related to cognition more broadly.

We analyzed behavioural measures (non-social and social cognitive scores) and resting-state functional magnetic resonance imaging (fMRI) data from the 'Social Processes Initiative in Neurobiology of the Schizophrenia(s) (SPINS)' study (248 stable participants with SSD and 172 healthy controls, ages 18-55). Three gradient components are extracted from parcellated connectomes (Ji et al., 2019; Margulies et al., 2016) and are then correlated with 6 non-social and 8 social cognitive measures. Next, by using partial least square correlation (PLSC; Krishnan et al., 2011), we decomposed this correlation pattern into uncorrelated dimensions that best capture their associations. In PLSC, each dimension is composed of 1) two sets of latent variables, which represent the participants on this dimension, with respect to the two sets of variables (i.e., behavioural and gradients), and 2) two sets of variable loadings, which describe how they contribute to this dimension. To examine how a dimension is related to clinical measures, including functioning, quality of life, and symptoms, in SSD, we performed Pearson's correlation tests (with false discovery rate correction) between these measures and the two sets of latent variables.

PLSC analysis identified one significant dimension (explaining 67.4% of the variance) as determined by the permutation test ($p < .001$). This dimension differentiated the healthy controls from the participants with SSD and is characterized by a positive correlation between network differentiation and general cognitive performance (i.e., both social and neuropsychological). Specifically, the cognitive deficits in SSD are related to decreased differentiation between lower- and higher-order networks (Gradient 1), between different lower-order networks (i.e., auditory and sensorimotor vs. secondary visual) (Gradient 2), and between the lower-order networks and striatum (Gradient 3). Furthermore, this dimension was positively correlated with frequencies of negative symptoms in SSD.

In this study, we used PLSC to identify cognition-related differences in network hierarchy. These results suggest a potential role of decreased differentiation of brain networks in functional impairment in SSD; more specifically, the decreased differentiations between the lower- and higher-order networks and between different lower-order networks are associated with both social and non-social cognitive impairments in SSD.

Fine-Scaled Connectivity Gradients Improve Brain-Behavior Predictions
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Dimensionality reduction techniques are increasingly utilized to characterize meaningful organizational principles within high-dimensional brain connectivity data. The dimensions of such low-dimensional representations - so-called connectivity gradients - capture topographical patterns of intrinsic brain organization. Their calculation usually relies on a n-by-n affinity matrix that is constructed by pairwise connectivity between n nodes.

The computational cost increases exponentially with the number of nodes, and for high-resolution data spaces such as the 90,000 grayordinates of the Human Connectome Project, more than 100GB of memory is required for the calculation. This renders voxel-wise calculation of gradients often intractable on consumer hardware, typically requiring users to downsample the data, e.g. through a parcellation strategy. While parcellation and the entailed data averaging can increase signal-to-noise ratio, concerns about the loss of detail and the appropriate choice of parcellation remain.
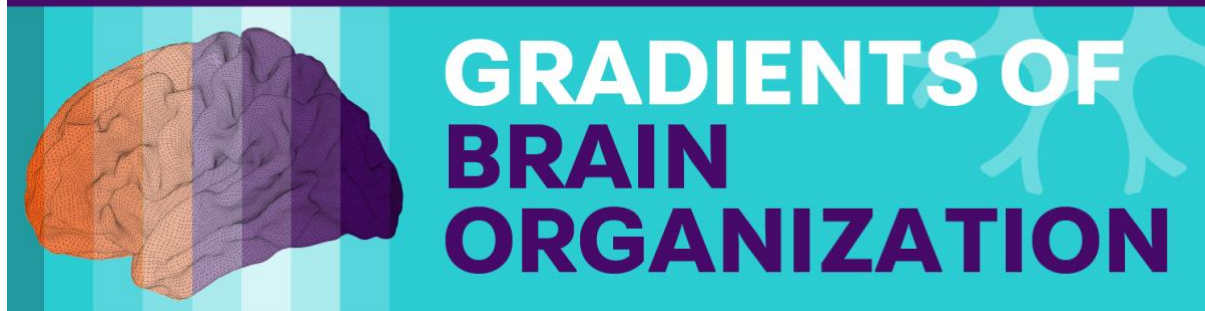
GRADIENTS OF BRAIN ORGANIZATION

Here, we propose a computationally efficient approach to establish high-resolution connectivity gradients, leveraging consumer-grade hardware. At its core, the approach uses a subset of connectivity targets to approximate the underlying connectivity structure at full scale. We evaluated our approach on the group and individual level, using two different datasets: the Human Connectome Project (HCP) and the Enhanced Nathan Kline Institute - Rockland Sample (NKI-RS). We evaluated the performance of different connectivity targets based on parcellations and individual vertices, randomly and uniformly distributed across the cortex. We quantified the spatial similarity (Spearman's ρ) between approximated gradients (Gapprox) and gradients based on the full connectivity matrix (Gfull_fc). Furthermore, we studied the practical implications of gradients based on parcellated data by comparing the predictive performance (age and intelligence) to parcellated fine-scale gradients.

The spatial similarity between Gapprox and Gfull_fc increased with the number of connectivity targets used to calculate the approximated gradients. Remarkably, when using 1000 Schaefer parcels as connectivity targets (~1.7% of the full connectivity matrix), the average spatial similarity across 25 connectivity gradients was $\rho > 0.85$. Increasing the number of targets further to 3000 uniformly sampled vertices (~5% of the full matrix), an average spatial similarity $\rho > 0.98$ was achieved with <10% computational time and memory usage, compared to the calculation of Gfull_fc. On the individual level (HCP, n=100), reliability and discriminability analysis confirmed the repeatability and the preservation of individual features for Gapprox. Importantly, in brain-behavior prediction using a lifespan cohort (NKI-RS, n=313, age 6-86y), averaged fine-scale gradients Gapprox with parcels outperformed gradients calculated from parcellated time series. This was observed for both age and intelligence across various parcellations.

Overall, approximation of full-scale connectivity gradients is computationally efficient, feasible on commodity hardware, showing a $\rho > 0.98$ spatial similarity with the full gradient results at a fraction (~10%) of the computational costs. Importantly, calculating large-scale gradients preserves more relevant information for predicting age and intelligence as gradients calculated from parcellated data. The high fidelity with gradients based on the full connectivity matrix paired with its ability to run on consumer hardware can both democratize this powerful approach and advance new insights across a range of applications.
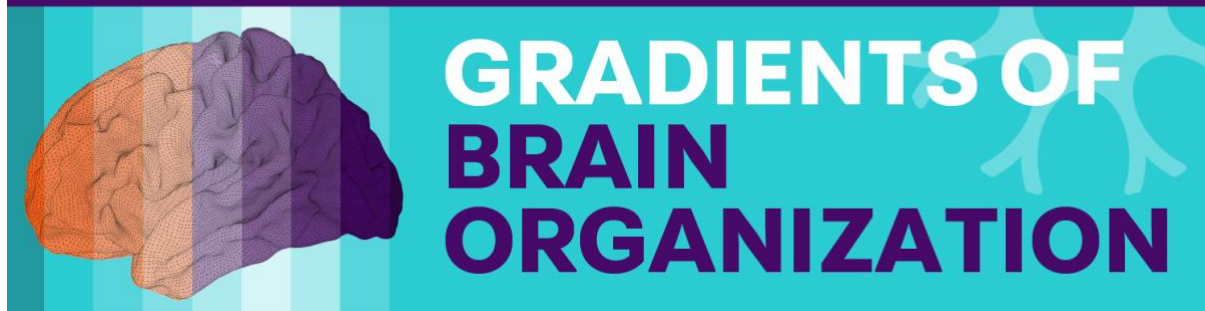
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System-level cortical maturation links to adolescent resilience to adverse life events

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Adolescence is a period of increased brain reorganization that is essential to biological and psychosocial maturation, but also to mental health (Paus et al., 2008). Normative adolescent brain maturation as captured via neuroimaging follows two main modes: 1) conservative strengthening of initially strong connections, or 2) disruptive remodeling, i.e. strengthening of initially weak connections and vice versa (Váša et al., 2020). While adverse experiences and psychopathological processes can alter maturational trajectories (Stenson et al., 2021), adolescent reorganization may also hold potential for flexible adaptation to risk factors. Thus, normative maturation facilitating psychosocial skills may also aid well-being through resilience to adversity.

We analyzed age-related changes in microstructural profile covariance (MPC; Fig. 1A) and resting-state functional connectivity (FC; Fig. 1B) in a longitudinal cohort of individuals aged 14-26 (n=295; 512 scans; 50.8% female). MPC reflects inter-regional similarity of intracortical profiles based on myelin-sensitive magnetic transfer (MT) data sampled at ten cortical depths. We first identified maturational modes by correlating the whole-brain MPC and FC patterns of each region at age 14 with the age-related changes of these patterns (14-26y; computed via edge-wise linear mixed effect models; Fig. 1C). Positive correlations indicate conservative and negative correlations disruptive development (FDR<0.05). Next, we investigated whether observed maturational patterns may contribute to resilience to adverse life events. From the total cohort, we drew a sub-sample (n=281) of individuals who reported adverse life experiences in the past 18 months. Conceptualizing resilience as adaptation to adversity, individuals were matched based on their adversity load and allocated to either high (n=88) or low resilient (n=89) groups based on reported well-being scores (top or bottom 33%, respectively; Fig. 2A). Structural and functional brain maturational modes were contrasted between the two groups via Fisher's z differences.

Our work describes topologically heterogeneous patterns of structural and functional maturational modes (Fig. 1D) and differential associations with resilience. We observed disruptive development of MPC in frontal and parietal cortical areas, and conservative development in sensory, paralimbic, temporal and medial frontal regions. Linking structure to function, we found parallel conservative development in regions involved in sensory- and attention-related processes. Default mode and frontoparietal networks showed both cross-modal disruptive rewiring and a structure-function divergence, in which structure showed conservative but function disruptive developmental patterns (Fig. 1E).

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Last, we found that individuals who maintain better well-being after exposure to adverse life events showed overall less conservative and more disruptive functional maturational patterns, indicating increased functional network rewiring during development. Effects were smaller for structural patterns and suggested a potential benefit of disruptive MPC development only in regions where change occurs in parallel with functional change (Fig. 2B).

Our longitudinal findings show overlapping but distinct patterns of structural and functional reorganization during adolescence. Cross-modal cortical transformations and structure-function decoupling in maturational modes were observed in association and paralimbic cortex, which are known to show protracted plasticity associated with both sociocognitive refinement and psychopathological alterations (Sydnor et al., 2021). Our findings suggest that brain remodeling throughout adolescence is especially pronounced in individuals showing better adaptation to adverse life events, and may thus facilitate resilience. This observation is in line with current psychological constructs of resilience as an adaptive, flexible process (Kalisch et al., 2017).

Body mass index-dependent shifts along large-scale gradients in human cortical organization explain dietary regulatory success
Remi Janet, Queens University, Kingston, Canada

People differ in their ability to adopt and maintain a healthy diet, even if they explicitly have the goal of eating healthily (Hare et al., 2009, 2011; Hutcherson et al., 2012). Recurrent failures to exercise dietary self-control can result in weight gain and severe long-term consequences for personal and public health (Stephenson et al., 2021; Tremmel et al., 2017). In 2018, 63.1% of Canadian adults were classified as overweight or obese, yielding increased health risks (Statistics Canada, 2019). Why do many people struggle to regulate their diets?

We propose that the brain might solve the problem of flexible, goal-consistent dietary choices by adopting – and shifting – brain states in a multi-dimensional space of principal dimensions of brain variation (gradients). Previous evidence of altered gradient organization due to increased body mass index (BMI) highlights the promise of this framework to study long-term dietary success (Park et al., 2021). Here, we tested whether shifts in brain states along large-scale gradients predict short-term regulatory success in a laboratory food task and how BMI moderates this link. Participants (N=123, 27±6.2 years, 84 f, BMI: below 35) performed an established fMRI food choice task (Hare et al., 2009).

They made choices under a non-constraint (NC) and health-focus condition (HC). We projected task-evoked brain states measured under both choice conditions in a three-dimensional space of established cortical principal gradients (Margulies et al., 2016). These gradients (manifolds) were originally determined from the decomposition of resting state data from the Human Connectome Project.

 We show that shifts in individuals' brain states during natural and regulatory dietary choice (NC to HC, Euclidian distance) predict variance in individuals' dietary regulatory success observed in the laboratory food task ($r2=0.33$, $p=0.015$). Results revealed a significant interaction effect between the magnitude of these goal-related neural shifts in the gradient space and BMI ($\beta=3.12$; $p=0.016$, CI [0.60, 5.65]). Compared to overweight and obese individuals, leaner participants (BMI <= 25) showed smaller shifts to achieve regulatory success, suggesting that their natural and regulatory dietary brain states are more similar (closer together) in the gradient space.

We show that variance in dietary success across people can be understood as changes along neurocognitive functional hierarchies. Our results indicate how cognitive functions like dietary control might emerge from the cortex through varying similarities along established macroscale patterns of organization.

The Structural Organization of the Zona Incerta Investigated Using 7 Tesla Diffusion MRI

Roy A.M. Haast, Aix-Marseille University, Marseille, France

The zona incerta (ZI) is a deep brain region that remains poorly understood. The ZI and its surrounding structures have been speculated to play crucial roles in a wide range of brain functions and have been considered as potential targets for neuromodulatory therapies. Recent advancements in high-resolution magnetic resonance imaging (MRI) at ultra high-field strength (7 Tesla; 7T) have allowed for direct visualization of the human ZI and differentiation of its substructures. In this study, we aimed to explore the internal organization of the ZI based on its connectivity using 7T diffusion MRI (dMRI) data from the Human Connectome Project (HCP) and to investigate its potential role in overall brain functioning.

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To investigate the structural connectivity between the ZI region (ZIR) and the cortex, we used minimally preprocessed anatomical and dMRI data from 173 individuals from the HCP. The ZIR and cortical regions were defined using previously derived probabilistic and volumetric parcellations (HCP-MMP1.0) and mapped to each subject's native space. We employed probabilistic tractography using FSL's probtrackx, with tractography seeded from the ZIR and targeting the cortical regions of interest. The resulting tracts were then transformed to a common template space (MNI152NLin6Asym) to enhance inter-subject overlap of the ZIR. Group-average and subject-wise voxel-wise gradients within the ZIR were extracted using BrainSpace from the corresponding connectivity matrices (with edges representing streamline count), and the group-wise gradients were projected onto the cortex to generate gradient-weighted cortical maps. These maps were then compared with other cortical properties within the NeuroMaps database.

Our findings revealed the presence of a principal gradient along the anteromedial to posterolateral axis of the ZIR, explaining 40% of the variance. This principal gradient effectively distinguished the ZIR's connectivity with motor regions from its connectivity with non-motor regions. Notably, the highest values in the gradient-weighted cortical maps predominantly corresponded to the somatomotor network of the brain. Additionally, a second gradient (explaining 21% of the variance) separated the more central portion of the ZIR from the rest, with a preferential connectivity to the prefrontal cortex and frontal/temporal pole. These results were consistent with recent findings using tract tracing techniques. Both gradients were reproducible across individual subjects with highly overlapping transition areas. Furthermore, correlation analyses revealed significant similarities between the gradient-weighted cortical connectivity maps and the first principal component of NeuroSynth-derived cognitive activation, while the second gradient showed unique associations with cortical properties measured using resting-state magnetoencephalography (MEG), such as theta band activity.

These findings provide further evidence for the involvement of the ZIR in mediating motor-related processes and strengthen the link between its structural connectivity patterns and its potential as a target for neuromodulatory interventions in movement disorders. Moreover, our results suggest that the ZIR may exert regulatory influence on regions beyond those involved in motor functions, impacting their engagement in various cognitive processes, including memory, attention, and cognitive control networks, as indicated by the associations with cortical properties measured using resting-state MEG, such as theta band activity.
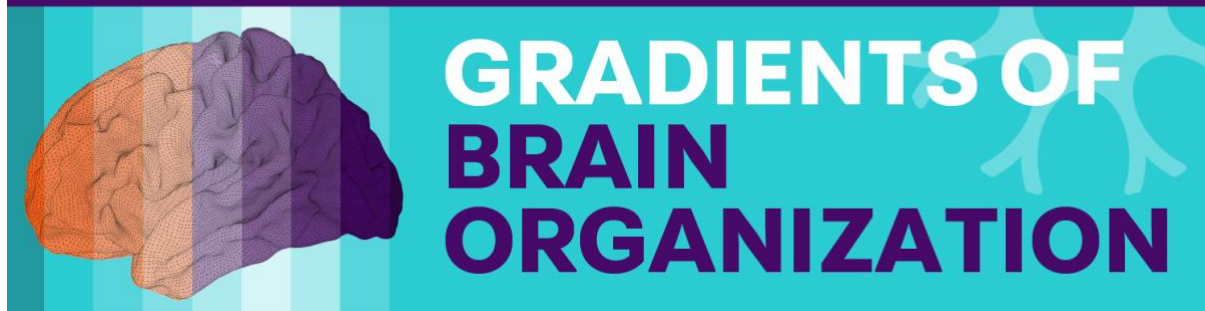
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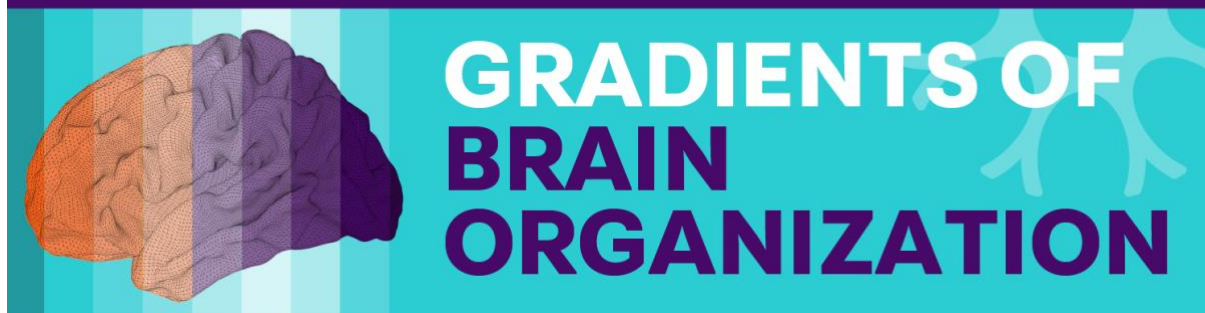
A Shifting Role of Thalamocortical Connectivity in the Emergence of Large-Scale Functional Brain Organization during Early Lifespan

Shinwon Park, IBS Center for Neuroscience Imaging Research, Sungkyunkwan University, Seoul, South Korea

How does the brain acquire specific functions across different areas (i.e., functional specialization), and how do functionally specialized areas organize major processing architectures such as cortical hierarchy across development?

While the interplay between intrinsic (i.e., genetic patterning) and extrinsic (i.e., sensory experiences relayed through thalamic connections) mechanisms have been, for long, considered critical for such developmental processes during the embryonic stages, our understanding of the postnatal brain development is still limited. Given thalamocortical circuitry plays a fundamental role in sensory processing and continues to evolve throughout the lifespan, it may play a critical role in shaping functional organization throughout development. Accordingly, in this study, we examined the developmental effects of thalamocortical connectivity on large-scale functional brain organization across infancy, childhood, adolescence, and young adulthood.

We employed connectopic mapping to chart the gradually changing functional relationship between thalamus and neocortex in two developmental cohorts: 1) developing Human Connectome Project (HCP) (195 infants [39.7 ± 3.0 weeks]), and 2) HCP development (603 participants [14.8 ± 3.9 years]). We then employed mechanistic approaches, such as genetic transcriptomic association analysis and developmental brain simulation based on generative network modeling, to interpret the developmental changes. Through thalamus-centered (e.g., core and matrix genes) and whole-brain (i.e., Allen Human Brain Atlas) analyses, we delineated subcortical-cortical gene influences, and then leveraged generative network modeling to simulate brain development. Finally, perturbing the network simulations allowed us to identify an age window contributing to the emergence of large-scale cortical hierarchies.

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The development of thalamocortical connectivity showed diverging patterns across age, indicating a developmental change in the relationship between the thalamus and cortical functional organization. During infancy, thalamocortical connectome topology showed strong anchors in low-level sensory regions while the other end was spread out across undifferentiated higher-order cortical regions, indicating that the thalamocortical connections lay the basis for the development of cortical hierarchy. We also found a significant interaction with cortical genes involved in developmental processes only during infancy. During childhood to adolescence, these thalamic projections undertake a unique role of differentiating between internally- and externally-oriented functional processes, suggesting the emergence of mature functional systems. Specifically, the salience network forms a stable anchor that differentiates between external-oriented networks such as dorsal attention, visual and sensorimotor networks on one gradient, and the default mode network on the other gradient. Moreover, this differentiation reflected the distinct patterns of underlying thalamic projections based on the relative density of 'core' and 'matrix' cells.

Finally, we demonstrated that the thalamocortical connectivity is a major player in scaffolding the emergence of a continuous internal-external functional brain stream (i.e., "functional gradient" by Margulies, et al. PNAS 2016) and modular structures using generative network modeling. Specifically, our perturbation analysis revealed its highest influence in later age groups (i.e., above 12 years), particularly in the development of cortical hierarchy, including internal processing areas such as the default mode network.

Our findings provide compelling evidence of the active role of thalamocortical connectivity in shaping large-scale functional brain organization, emphasizing its significant impact across the different developmental stages.

Multimodal gradients of the human basal forebrain
Sudesna Chakraborty, Western University, Canada

The basal forebrain (BF) is a collection of subcortical nuclei which provide the major sources of acetylcholine to the neocortex and hippocampus. In the past decade, cell type specific labelling techniques have led to several major revisions in our understanding of the morphology and function of BF cholinergic neurons. First, the BF cholinergic neurons are enormous. Individual cells with >1000 axonal branches have been observed in mice. Second, the organization of cholinergic neurons, with respect to the position of their cell bodies within the BF and the cortical targets of their projections, appears to reflect a topography. Moving from anteromedial to posterolateral nuclei of the BF, cholinergic neurons differ in terms of their preferred cortical projection targets.

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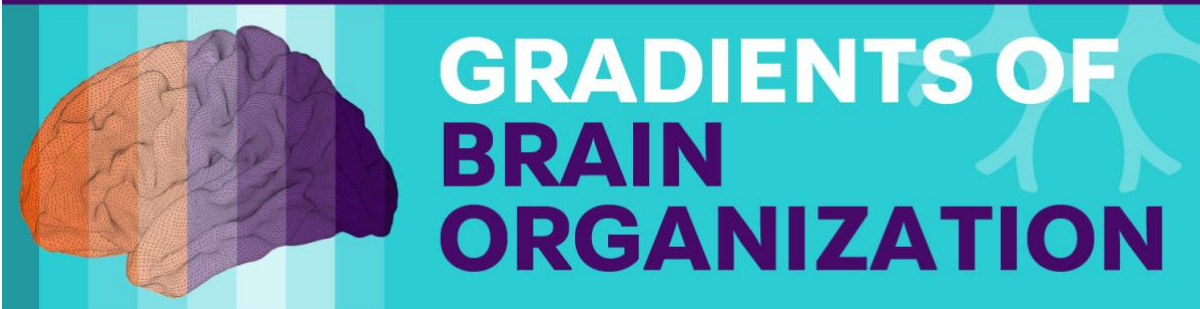
Despite the fact the BF cholinergic system is highly conserved across mammalian species, humans have evolved a much larger cerebral cortex compared to mice. How are the BF cholinergic neurons organized in the human brain? Does this organization reflect their functional and structural integration with the cortex?

We addressed these questions using multimodal imaging in humans; we used Human Connectome Project (HCP) 7T diffusion MRI and resting state fMRI data. Additionally, we employed a PET radiotracer targeting the vesicular acetylcholine transporter (VAChT) to quantify the locations and density of presynaptic BF cholinergic terminals with cell type specificity. Similar to the topography of BF cholinergic projections observed in mice, we found that the human BF exhibits a gradient both structurally and functionally, broadly differentiating anteromedial from posterolateral nuclei. We then examined the interrelationship between gradients of structural and functional connectivity by calculating weighted residuals. moving from anteromedial to posterolateral BF, structural and functional gradients became progressively detethered, with the most pronounced dissimilarity localized in the nucleus basalis of Meynert (NbM)—a subregion which has undergone disproportionate phylogenetic progression in size and complexity in humans. We then examined where this detethering was most strongly expressed in the cortex. The result exhibited increasing dissimilarity moving from unimodal to transmodal cortex, with the highest dissimilarity overlapping primarily with the ventral attention network. We finally explored what may account for this detethering and observed that VAChT concentrations were highest in cortical areas exhibiting greater detethering. Cortical properties that further strengthened this spatial relationship included shorter geodesic distance to the BF and lower myelination (T1w/T2w ratio).

This study is the first to examine human BF connectivity using both structural and functional MRI in combination with molecular imaging. Our findings imply that the BF provides cholinergic innervation to the cortex in a topography characterized by branch complexity. In this architecture, the most highly branched cholinergic neurons may originate from the nucleus basalis of Meynert and innervate hubs of the ventral attention network—consistent with the role of these areas in orienting attentional resources throughout the brain. These findings will be of broad interest to researchers studying the human cortical connectome.

The Cellular Underpinnings of the Human Cortical Connectome
Xi-Han Zhang, Yale University

The functional properties of the human brain arise, in part, from the vast assortment of cell types that pattern the cortex. The cortical sheet can be broadly divided into functionally distinct networks, which are further embedded into processing streams, or gradients, that extend from the unimodal systems through the higher-order association territories.

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Initial work suggests a link between spatial patterns of cellular organization and in vivo properties of brain functioning observed in fMRI, thorough investigations of the cellular underpinning of functional organization properties remain uncharacterized. Here, using transcriptional data from the Allen Human Brain Atlas (AHBA) and single-cell data collected by Lake et al., we demonstrate that imputed cell type distributions are strongly spatially coupled to the in vivo functional organization of the cortex.

Functional network structure of the cortical sheet was characterized by 200 bilateral and roughly symmetric regions which can be further classified into 7 large-scale networks. Gradients of functional connectivity (FC) were derived using vertex-level FC matrices from 820 subjects in HCP, and mean gradient value of each region was assigned to each region. Microarray gene expression data were obtained from bulk tissue samples from 6 postmortem brains in AHBA. Single-nucleus droplet-based sequencing data obtained by Lake et al. were used to impute the cell type fractions in each bulk sample. The imputed cell types fractions were then mapped to each donor's cortical surface and aggerated across each region. Univariate relationships between the distribution of each of the 17 cell types and gradients were examined using the permutation method. Multivariate associations between combinational cell-type distributions and functional gradients were examined using the canonical correlation analysis. Support vector machines were trained to predict the functional network assignment of each cortical parcel based on fractions of 17 cell types within that parcel. The accuracy was assessed using F-2 score and recall, and statistical significance was evaluated against both theoretical probabilities and a permutation procedure that accounts for spatial autocorrelation.

One subtype of excitatory neuron (r=0.307, p-fdr<0.001) and VIP interneuron (r=0.309, p-fdr=0.011) were found preferentially distributed along the transmodal pole in the primary gradient (transmodal-unimodal), and PVALB interneuron (r=-0.367, p-fdr=0.009) preferentially distributed along the unimodal end of this gradient. Another subtype of excitatory neuron (r=0.375, p-fdr=0.009) associated with the second functional gradient, which is anchored within the unimodal cortices, peaked in the occipital lobe then extended through somatomotor-auditory territories. Linear combinations of the 17-cell type distribution were found to be highly correlated to the two gradients (r=0.524, p-spin<0.001; r=0.586, p-spin<0.001).

Indicating that cortical cytoarchitecture also follows the topography of canonical functional networks, an SVM trained from cell-type fractions of each parcel was able to accurately categorize somato-motor (p-spin<0.001), visual (p-spin=0.027), ventral attention (p-spin=0.037), and limbic networks (p-spin=0.006).

Friday, July 21 | 9 a.m. EDT   Jeanne Timmins Amphitheatre, The Neuro
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We demonstrate that imputed cell type distributions are strongly spatially coupled to the functional organization of the cortical sheet. Spatially heterogeneous cortical cytoarchitecture follows the two primary macro-scale functional gradients. Distinct cellular fingerprints were evident across functional networks, and a classifier trained on the distributions of post-mortem cell types can predict the large-scale functional network allegiance of post-mortem tissue samples within cortical parcels. These data indicate that the in vivo hierarchical organization of the cortical sheet is reflected in the spatial variability of its cytoarchitecture.

Is Thalamocortical Connectivity Reflected by Microstructural Features?

Alexandra John, Max Planck Institute for Human Cognitive and Brain Sciences, Germany

The thalamus is a diencephalic, bilateral, and highly heterogeneous structure that is extensively connected to cortical and subcortical regions. While in the cortex an association between structurally connected regions and structural covariance has been shown (Gong et al., 2012), implications for thalamocortical interrelations remain unclear. Here, we studied the link between thalamocortical structural connectivity, local intrathalamic microstructure, and global thalamocortical microstructural covariance.

Using diffusion-weighted imaging and quantitative T1 (qT1) data from the MICA-MICs dataset (N=50, age 29.54±5.62y; Royer et al., 2022), probabilistic tractography from thalamic seed voxels (left (L) 1068, right (R) 1029; resolution 2mm) to 100 ipsilateral cortical parcels (Schaefer et al., 2018) was computed and averaged to create a group-level structural connectivity matrix. The two main axes of thalamocortical structural connectivity were extracted by performing diffusion map embedding (Coifman & Lafon, 2006). To contextualize with intrathalamic microstructural features, the thalamic axes were correlated with a gene-expression map that reflects thalamic core- and matrix cell distributions (Müller et al., 2020), and intrathalamic qT1 as a proxy for myelin, while correcting for spatial autocorrelation (SA) using variograms (Burt et al., 2020). Next, we extracted qT1 values of thalamic voxels, and qT1 intensity profiles for cortical parcels sampled perpendicular to the cortical surface (Cruces et al., 2022). Depth-specific structural covariance matrices were generated by correlating thalamic (voxelwise) and cortical (parcelwise) qT1 measures. The correlation between gradient loadings and structural covariance was studied using the cross-depth average and according to cortical depth-specificity.

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The principal gradient (G1) of thalamocortical structural connectivity reflected a medial to lateral-central transitional axis, while for the secondary gradient (G2) one apex was located at the medial-anterior and medial-posterior thalamic pole, and the opposite apex intersected the thalamus anterior-laterally to central-medially. Projected onto the cortex, G1 revealed a paralimbic-to-somatosensory axis, while G2 dissociates posterior-to-anterior regions. G2 was correlated with the distribution of core-matrix cells in the left thalamus (Pearson's r=0.57, pSAcorr=0.03). We further found G1 correlated with intrathalamic qT1-intensity (L: r=-0.49, pSAcorr=0.026; R: r=-0.54, pSA=0.008). For G1, structural covariance correlated negatively with the inferior-anterior cortex regions and positively with superior-posterior regions. Moreover, the association between G1 and thalamocortical structural covariance varied across cortical depths.

We characterized variations of thalamocortical connectivity patterns across the thalamus and showed its links to intrathalamic microstructural and cellular variations. Further, extending on research in mice (Yee et al., 2022), we demonstrated that thalamocortical structural connectivity is linked to structural covariance in a depth-varying manner.

Longitudinal Neurotypical and Neurodivergent Gradients of Structural and Functional Brain Development

Alicja Monaghan, MRC Cognition and Brain Sciences Unit, University of Cambridge, UK

How do structural and functional cortical gradients vary over developmental time, both within and between individuals, and are these changes universal across neurotypical and divergent populations? To answer this, we derived structural (communicability from diffusion-weighted imaging) and functional (blood oxygen level development time-series from resting-state functional magnetic resonance imaging) gradients. To test the robustness of these gradients across neurodevelopmental profiles, we used two mixed-design developmental data sets. The first was a community-ascertained sample of 369 children aged between 6 and 17 years old at baseline, from the NKI-Rockland Sample Longitudinal Discovery of Brain Development Trajectories sub-study in Orange County, US. We reconstructed structural and functional connectomes for 193 children with a single timepoint, 116 with two, and 68 with three.

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The second data set consisted of children from the Centre for Attention, Learning, and Memory study in Cambridge, UK, aged between 5.20 and 18.58 years at baseline. This sample is enriched for neurodivergent children, with most referred for difficulties in attention, learning, and memory. We reconstructed structural connectomes for 403 children at baseline, and 129 at follow-up. We reconstructed functional connectomes for 256 children at baseline, and 127 at follow-up. We first derived group-representative structural and functional gradients, for each data set. In CALM, the first structural gradient differentiated between visual networks and the prefrontal cortex, the second between visual and frontoparietal networks, and the third between visual and default-mode networks. In terms of functional connectivity, the first gradient differentiated between visual and default-mode networks, the second between visual and ventral attention networks, and the third between dorsal attention and default-mode networks. These results were consistent in the NKI data set. Across both datasets, there are complex mappings between the structural and functional gradients. For example, in CALM the primary structural gradient, and to a lesser extent the secondary structural gradient were strongly positively correlated with the second functional gradient ($r = .414$, $p < .001$; $r = .787$, $p < .001$, respectively). Furthermore, the primary functional gradient was significantly correlated with both the secondary structural gradient ($r = -.471$, $p < .001$) and the third structural gradient ($r = .405$, $p < .001$). Across both datasets we then examined the divergence of individual-level gradients from group-level gradients, using manifold eccentricity, and estimated cross-section and longitudinal associations with age and cognition. We suggest several avenues for further analysis, such as linking individual differences in structural and functional manifold divergence with neurodevelopmental symptoms and using publicly available positron emission tomography data to examine how neurotransmitter distributions may bridge structural and functional brain organisation.

Diverging Asymmetry of Intrinsic Functional Organization in Autism
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Autism is a neurodevelopmental condition involving atypical sensory-perceptual functions together with language and socio-cognitive deficits. Previous work has reported subtle alterations in the asymmetry of brain structure and reduced laterality of functional activation in individuals with autism relative to non-autistic individuals (NAI). However, whether functional asymmetries show altered intrinsic systematic organization in autism remains unclear.

Here, we computed inter- and intra-hemispheric asymmetry of intrinsic functional gradients capturing connectome organization along three axes, stretching between sensory-default, somatomotor-visual, and default-multiple demand networks, to study system-level hemispheric imbalances in autism. We observed decreased leftward functional asymmetry of language network organization in individuals with autism, relative to NAI. Whereas language network asymmetry varied across age groups in NAI, this was not the case in autism,

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suggesting atypical functional laterality in autism may result from altered developmental trajectories. Finally, we observed that intra- but not inter-hemispheric features were predictive of the severity of autistic traits. In sum, our findings illustrate how regional and patterned functional lateralization is altered in autism at the system level. Such differences may be rooted in altered developmental trajectories of functional organization asymmetry in autism.

Development of Thalamocortical Connectivity During the Third Trimester
Stuart Oldham, Murdoch Children's Research Institute, Melbourne, Australia

Thalamocortical connections are vital for communication between sensory inputs and the cortex, and between cortical regions, which enables essential sensory, motor, emotive, and cognitive processes. These connections emerge early in brain development, and proper formation is crucial for healthy brain function. While thalamic function is traditionally assigned to its nuclear structure, recent work has identified a supra-nuclear axis of thalamic organisation encoding variations in cortical projections, neuronal morphology, and electrophysiology that extends along a medial-lateral axis. This gradient mirrors early developmental events and is linked to neurodevelopmental/neurological disorders, suggesting it is hallmark of early thalamocortical organisation.

To examine how thalamocortical axes form during early development, we used dMRI data from 313 neonates (median [range] age at birth = 39 [25.6-41.5] weeks; median [range] age at scan = 40 [29.3-44.7] weeks; 140 females) of the Developing Human Connectome Project. Probabilistic tractography from 800 thalamic seeds to 29768 cortical vertices (left hemisphere only) was conducted to create a thalamocortical connectivity matrix for each neonate. A term template was created from the 20 oldest neonates to act as a reference. PCA was performed on the template/individual matrices. Resulting principal component (PC) scores reflect axes/gradients of variation in cortical connectivity across thalamic seeds, while PC loadings reflect patterns of cortical connections associated with thalamic axes.

The primary component (PC1) explained on average 40.2% (SD = 3.31) of variance in individual thalamocortical connectivity matrices. In thalamic regions, the PC1 gradient varied along an anterior/medial to posterior/lateral axis, with corresponding cortical projections varying rostral-caudally. Divergence from the term template (measured by correlating individual and neonatal PC1 scores) was significantly correlated with scan age ($r = 0.713$, $p < .001$), with younger neonates the most dissimilar. To examine regional developmental changes in thalamocortical organisation, we correlated PC1 thalamic seed scores and cortical vertex loadings with scan age. Thalamic areas whose scores varied with age were located towards medial and lateral extremes, while cortical regions whose loadings varied with age tended to be in frontal/temporal/parietal association areas. Comparing term to preterm
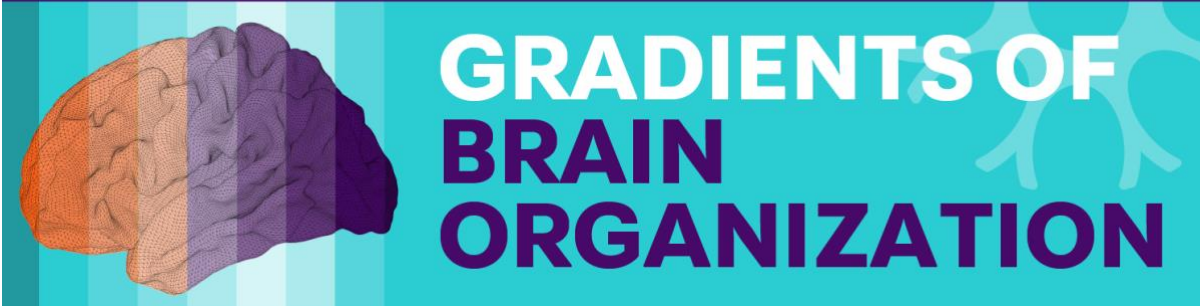
neonates scanned at term equivalent age, we only observed minor differences in PC1 scores in the medial thalamus.

The primary organisational thalamic gradient observed in adults is largely present at term birth. Connectivity became increasingly differentiated along this gradient during development, evidenced by lower ends of the gradient decreasing with scan age, while upper ends increased. Age-related effects in the cortex were concentrated in association areas, mirroring findings showing these areas are less mature but develop rapidly over the third trimester. Relative to term, preterm neonates had gradient differences in the medial thalamus, indicating altered thalamocortical connectivity in this area. Furthermore, cortical areas showing the strongest age-related effects have been linked to abnormalities in preterm birth. Preterm birth may disrupt the temporal sequence of events by which connections form along thalamic gradients. Assessing if disruptions along the primary thalamic gradient are related to preterm birth cortical abnormalities and testing the relevance of these thalamic disruptions to cognition and behaviour, is of interest for future work.

Functional Connectivity Gradients and Thought-Patterns in Schizophrenia - Negative Symptoms

Tal Geffen, Charité – Universitätsmedizin Berlin, Department of psychiatry and Psychotherapy, Berlin
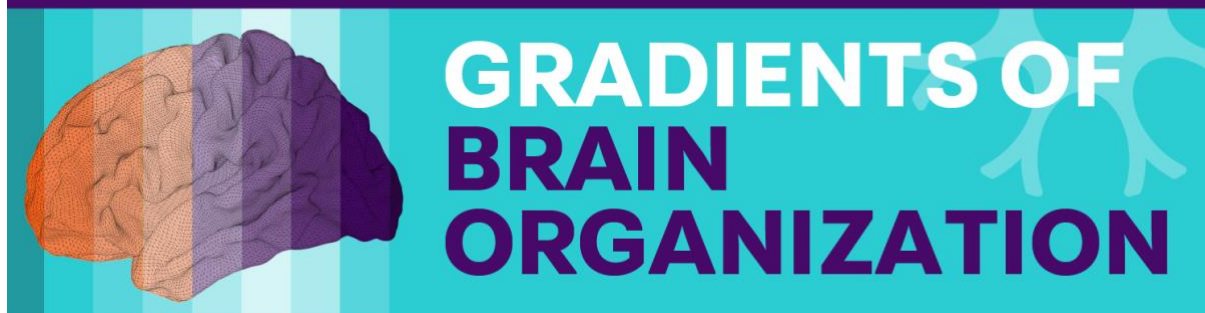
The study investigates the association between ongoing thought-patterns and macroscale neural connectivity patterns in patients with schizophrenia (SZP) negative symptoms and healthy controls (HC). Such an understanding could provide insights into the neural mechanisms underlying thought-patterns in SZP.

The study recruited 77 SZP and 66 HC, matched for age and sex, and scanned them using resting-state fMRI and Multi-Dimensional Experience Sampling. Principal Component Analysis (PCA) was used to extract six thought-pattern components (TPs), and cortical connectivity gradients were created using PCA. The TPs and three gradients were compared between the two groups, controlling for age, gender, and motion. Results were corrected for False Discovery Rate.

The SZP group had significant lower scores in TP1 (more episodic social thought in HC) and TP6 (more abstract spontaneous thought in HC) and higher scores in TP2 (intrusive and negative thoughts) than the HC group. In Gradient 1 (G1), differences were mainly from the DMN, visual, somatomotor, and attentional networks. SZP presented a more segregated pattern from the rest of the networks [all pFDR≤.02, t(138)≤ -3.5]. G2 was significantly shorter in SZP.

Our findings showed that TPs and brain organization differed between HC and SZP using gradient analyses in SZ for the first time. A pattern of DMN segregation from the rest of the networks, including the visual network, was seen among SZP. Attentional networks in SZP resembled more the visual network and had less similarity with DMN in G1; this fits findings from SZ studies with a focus on salience network-DMN connectivity.

Spatially Heterogeneous Structure-Function Coupling in Haemodynamic & Electromagnetic Brain Networks

Zhen-Qi Liu, McGill University, Canada

The relationship between structure and function is a central concept in systems neuroscience. While existing studies mainly focus on functional dynamics characterized by functional MRI (fMRI), it is known that BOLD responses do not directly reflect the underlying neural activity. Recent studies have also suggested a heterogenous correspondence between structural and functional connectivity, with stronger coupling in unimodal cortex and wicked correspondence in transmodal cortex. Altogether, it is necessary to have a more detailed understanding of structure-function relationship that takes into account both neurophysiological activity and regional heterogeneity. In this project we compare structural connectivity (SC) estimated using diffusion MRI with functional connectivity (FC) estimated using both neurophysiological (MEG-based) and haemodynamic (fMRI-based) recordings. We estimate regional patterns of structure-function coupling using a multilinear regression model that takes into account communication dynamics. We then explore the relationship between structure-function coupling patterns and cognitive systems, network features and cytoarchitectural profiles.

We used 33 subjects with full MRI and MEG acquisitions from the Human Connectome Project (HCP) to estimate the structural connectivity (SC), BOLD functional connectivity (BOLD-FC), and MEG functional connectivity (MEG-FC). MEG recordings were preprocessed using Brainstorm, and connectivity matrices were estimated using amplitude envelope correlation (AEC) for the six canonical electrophysiological bands (delta, theta, alpha, beta, low-gamma, high-gamma). Connectivity matrices were parcellated into the 400-node Schaefer atlas. Group consensus matrices were generated for each modality and frequency band. Multilinear regressions incorporating spatial, routing, and diffusion properties of the network were used to evaluate the extent of structure-function coupling. The coefficients of determination (adjusted R-squared) were used to quantify the coupling between structural and functional networks.

The present report comprehensively quantifies patterns of structure-function coupling across the neocortex using both MEG and fMRI. We found that region-resolved models that allow for local heterogeneity better capture structure-function relationships for both BOLD-FC and MEG-FC, showing a consistent pattern of stronger coupling in slower and intermediate frequency bands. Structure-informed communication metrics were used as predictors, and their relative contributions were calculated using dominance analysis, showing distinct enrollment of potential communication protocols across frequency bands. Across BOLD-FC and MEG-FC frequency bands, we discovered that structure-function coupling is highly organized across the cortex, with greater structure-function coupling in unimodal cortex and lower coupling in transmodal cortex, tracing out the archetypal sensorimotor-association axis.

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Further into the biological basis, we found that structure-function coupling also depends on regional differences in laminar differentiation estimated using the BigBrain histological atlas, with most prominent values in intermediate layers, corresponding to the granular layer IV.

In summary, we provided a comprehensive benchmark of the correspondence between dMRI-derived anatomical connectivity and functional connectivity across haemodynamic (fMRI) and electromagnetic (MEG) canonical frequency bands. We find robust evidence that structure-function coupling is systematically organized across the brain, and parallels variations in cytoarchitecture. These results set the foundation for studying structure-function coupling as a phenotype of brain organization and open the door for multi-modal studies of structure-function relationships.

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