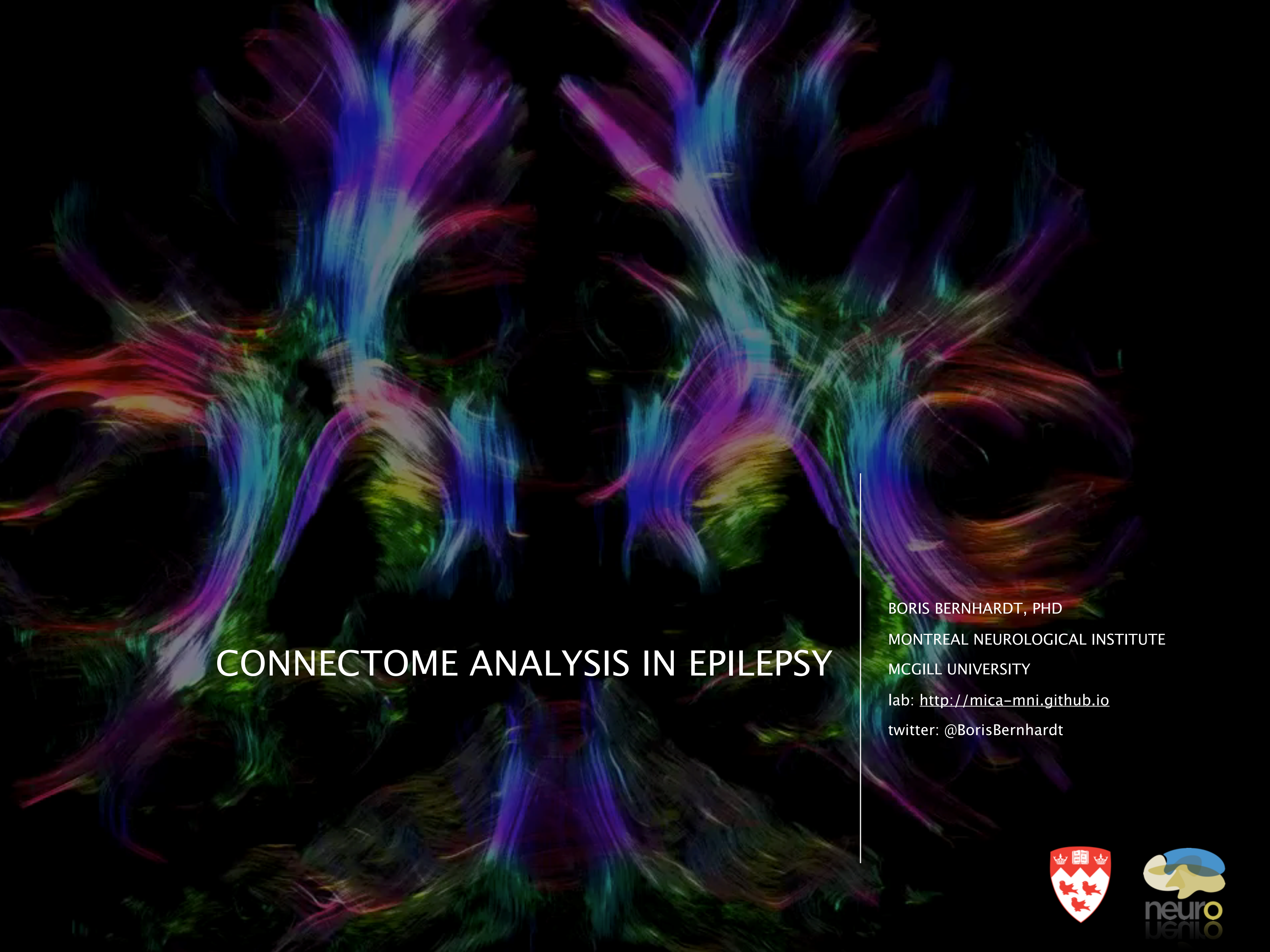

CONNECTOME ANALYSIS IN EPILEPSY

BORIS BERNHARDT, PHD

MONTREAL NEUROLOGICAL INSTITUTE

MCGILL UNIVERSITY

lab: http://mica-mni.github.io

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PRESENTER DISCLOSURE

FACULTY: BORIS BERNHARDT
RELATIONSHIP WITH COMMERCIAL INTEREST: NONE
HONORARIA: NONE
CONSULTING FEES: NONE
OTHER NONE

DISCLOSURE OF COMMERCIAL SUPPORT:

NONE

MITIGATING POTENTIAL BIAS:

N/A

WHY STUDY CONNECTIVITY?

WHY STUDY CONNECTIVITY?

American Epilepsy Society

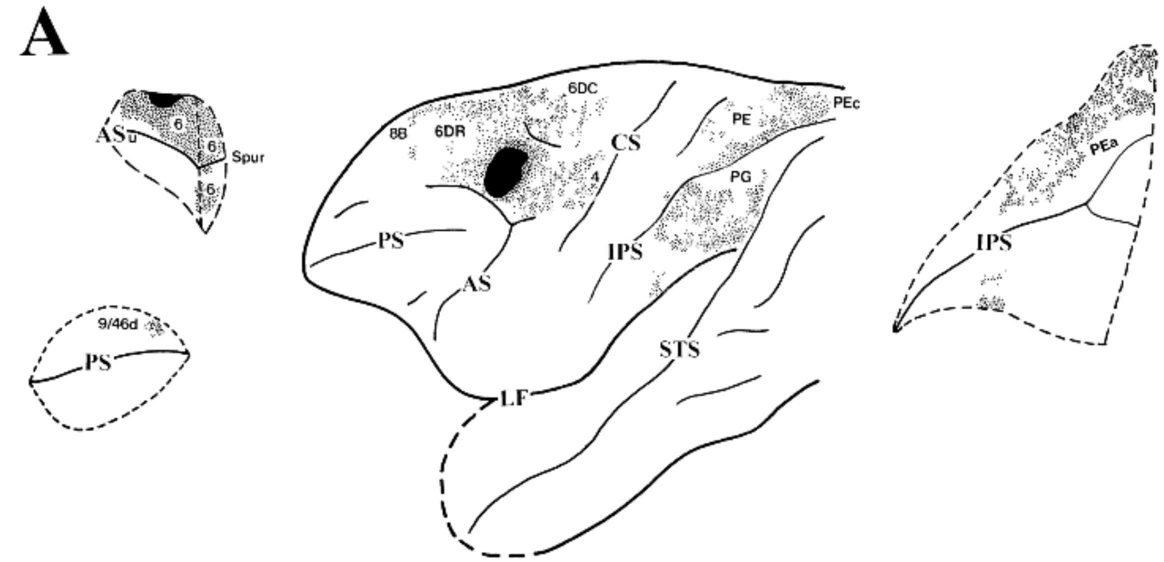
HOW TO MEASURE BRAIN CONNECTIVITY?

(ANIMAL) CONNECTIVITY

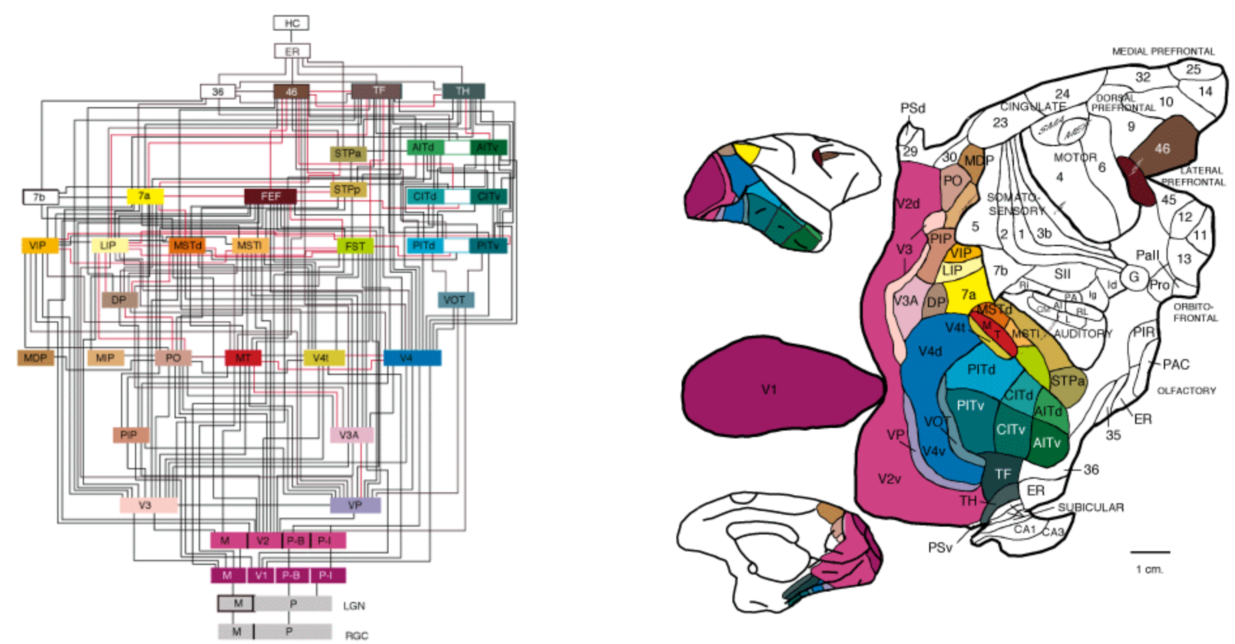
ANATOMICAL CONNECTIONS: THE WIRING BETWEEN REGIONS

CLASSICALLY DERIVED FROM TRACT-TRACER STUDIES

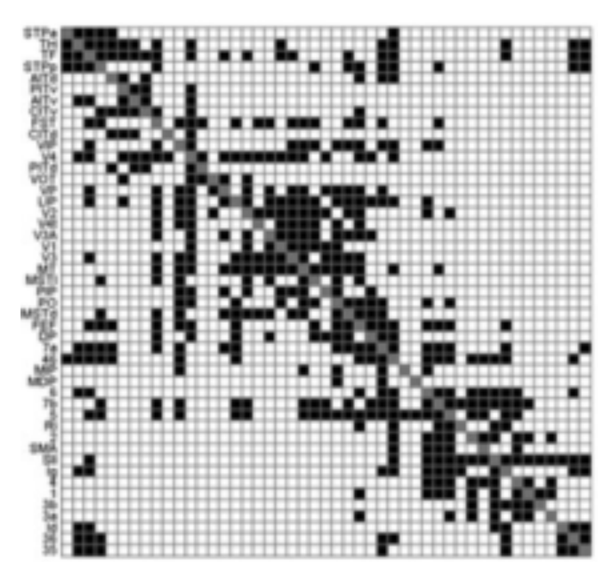
INVASIVE, CAN ONLY BE PERFORMED IN ANIMALS



Petrides & Pandya, 1999, EJN



Felleman and Van Essen, 1991, Cerebral Cortex



Stephan and Koetter, 2000, CoCoMac

HUMAN IN-VIVO CONNECTIVITY

MRI KEY MODALITY
TO APPROXIMATE BRAIN CONNECTIVITY

NON-INVASIVE

HIGH-RESOLUTION

WHOLE-BRAIN

3-DIMENSIONAL

FUNCTIONAL & STRUCTAL CONNECTIVITY

DIFFUSION MRI CONNECTIVITY

IDEA:
FOLLOW PATHWAYS
OF UNHINDERED WATER DIFFUSION

+
PROBES
WM CONNECTIVITY

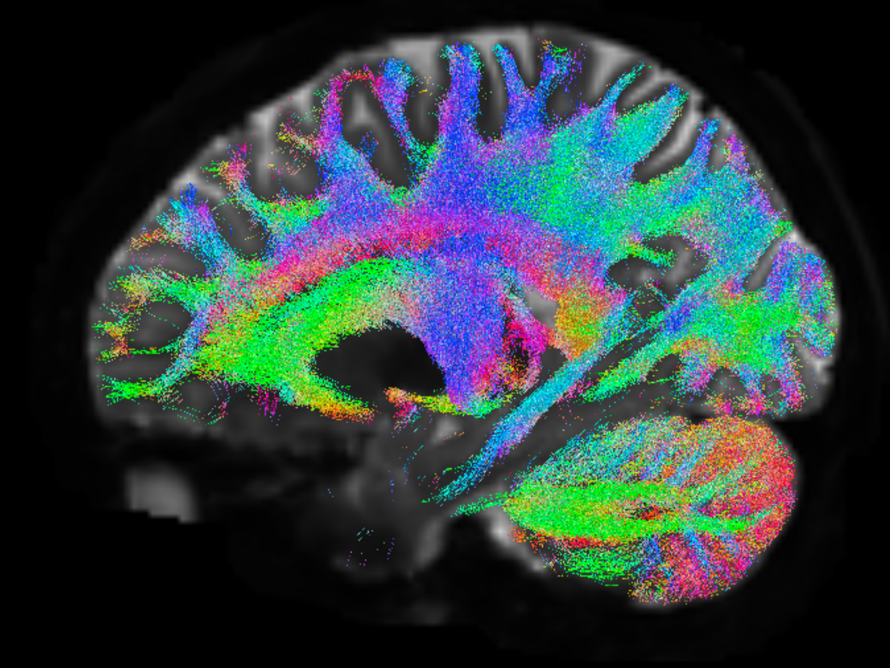
DIFFUSION PARAMETER
ANALYSIS CAN BE PERFORMED AS WELL

–

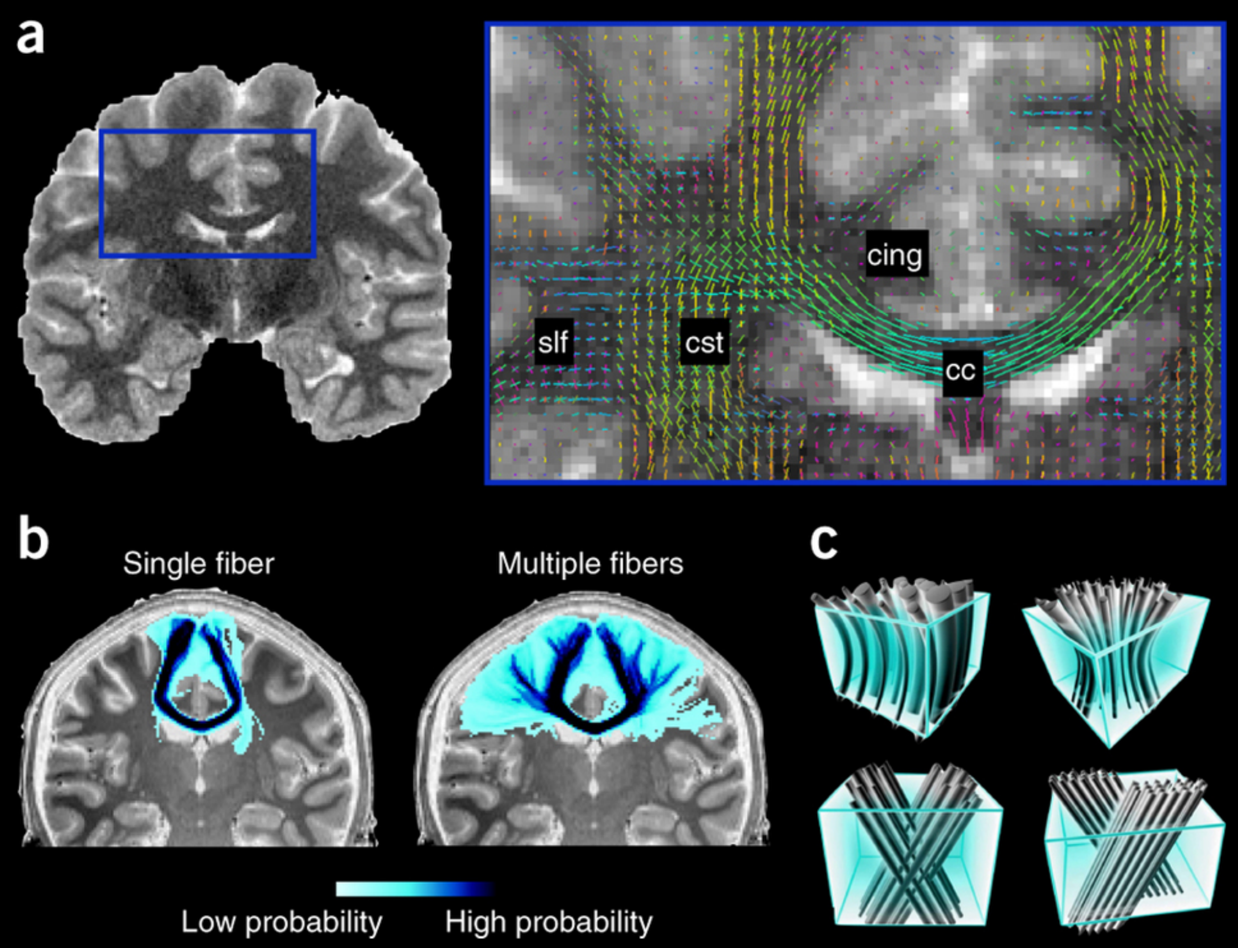
CHALLENGES IN REGIONS OF
FIBRE CROSSING AND UNCERTAINTY

DISTANCE BIAS

VALIDITY IN PATHOLOGICAL
REGION UNCLEAR



SINGLE SUBJECT (HCP)



Jbabdi 2015 Nature Reviews Neuroscience

RESTING-STATE fMRI CONNECTIVITY

IDEA:
CORRELATE SPONTANEOUS BRAIN ACTIVITY

+
COST-EFFECTIVE, REPRODUCIBLE

INDIVIDUALIZED

REGIONAL AND INTER-REGIONAL

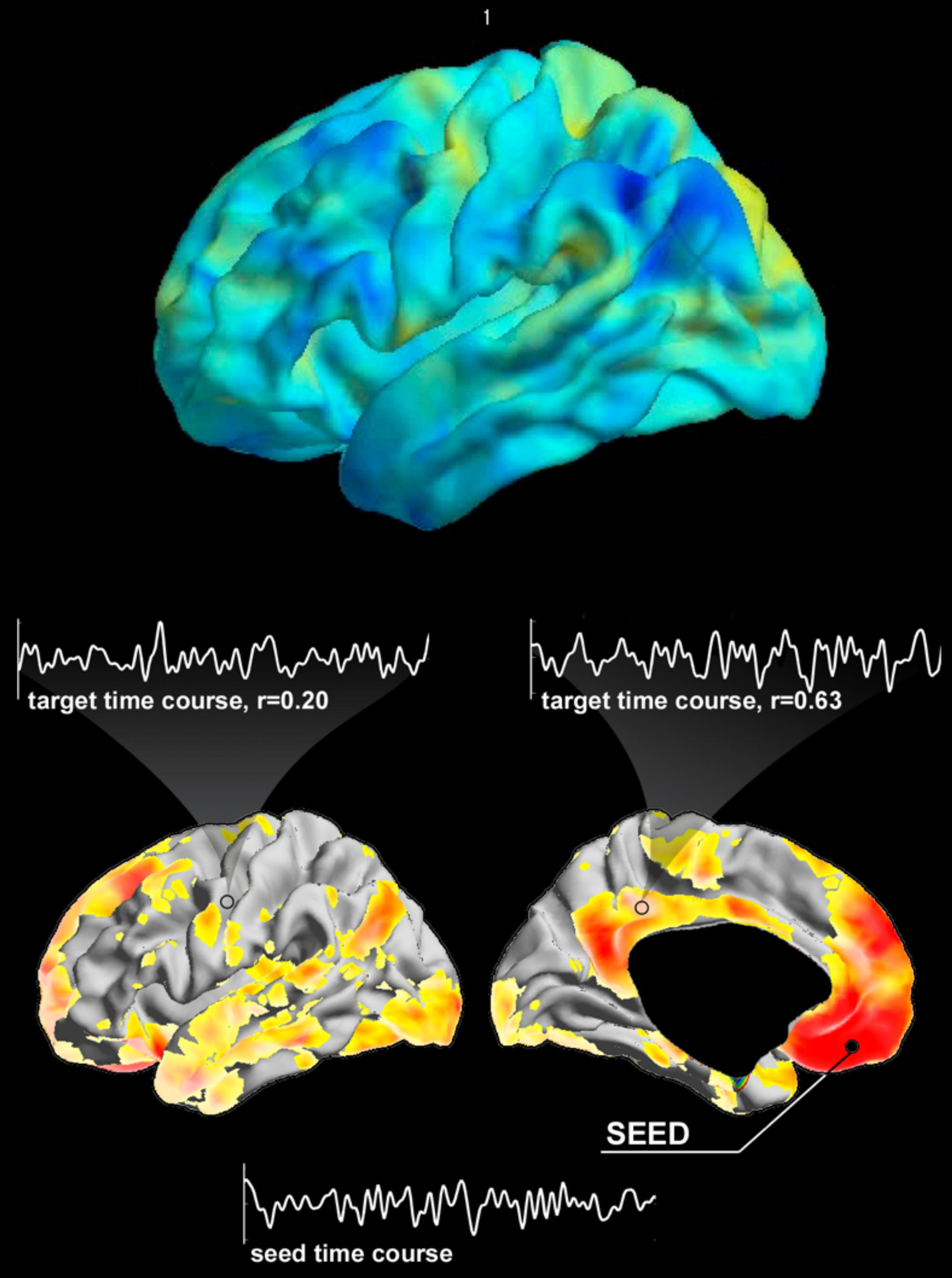
SEEDING FROM GM

CORRELATION WITH MENTAL STATES & INDUCTION

–
EFFECTS OF PHYSIOLOGY + MOTION

INDIRECT CONNECTIONS

CORRELATION WITH MENTAL STATES & INDUCTION



MRI COVARIANCE ANALYSIS

IDEA:
CORRELATE MORPHOLOGICAL INDICES ACROSS SUBJECTS

+
COST-EFFECTIVE, REPRODUCIBLE

DIRECT SEEDING FROM GREY MATTER POSSIBLE

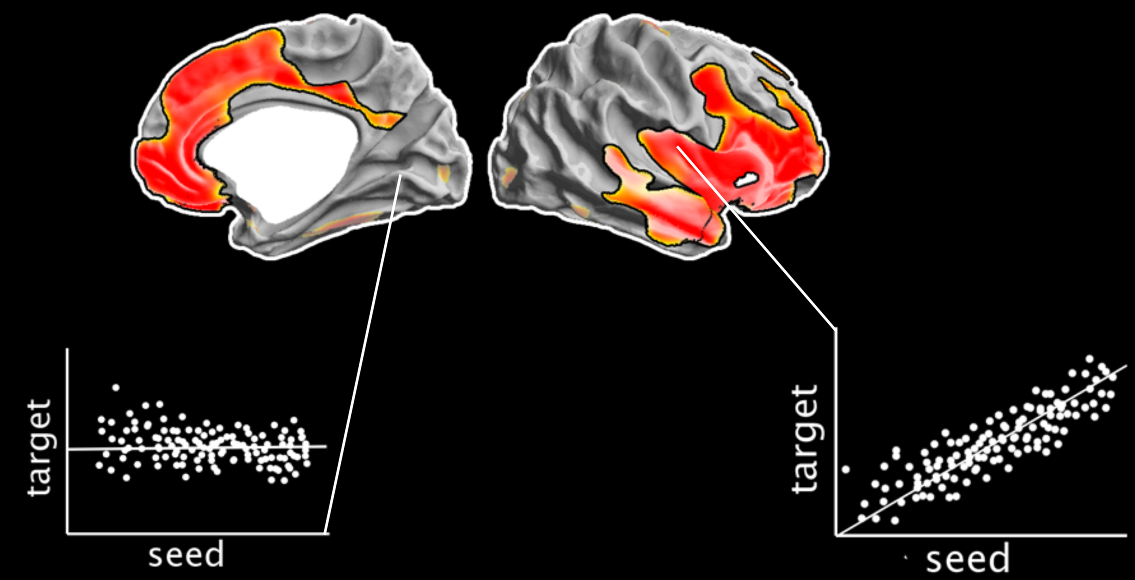
SIMPLE PREPROCESSING AND MODELLING

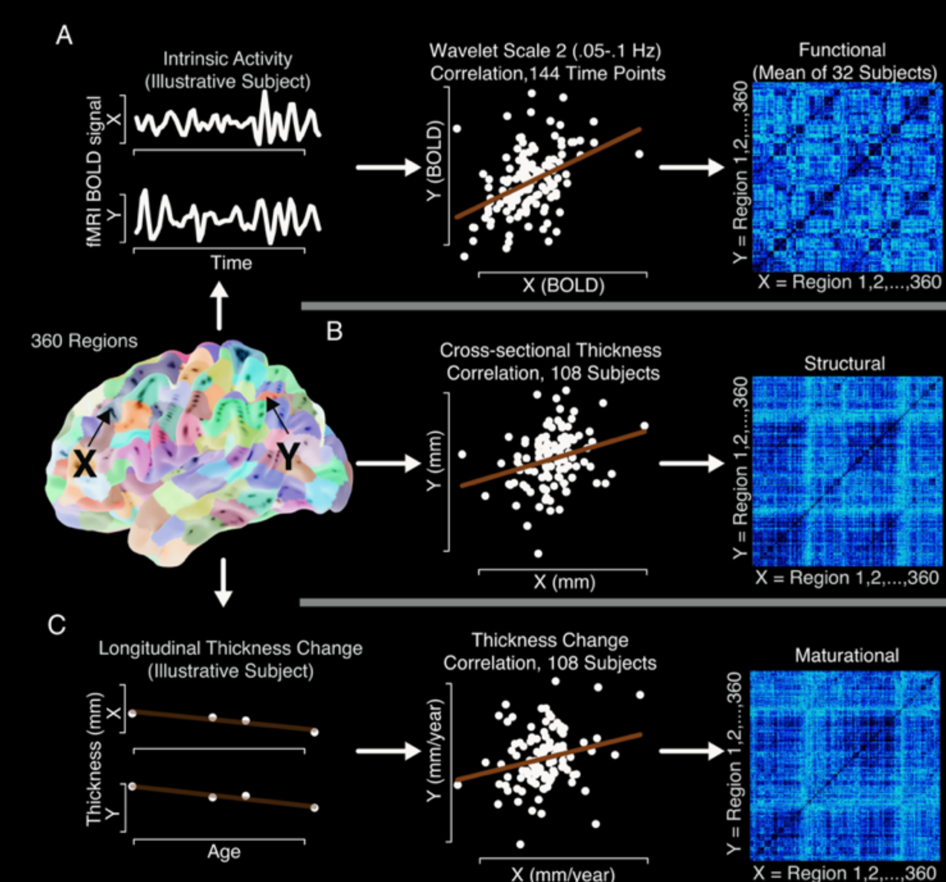
–

ONLY GROUP-WISE

RELATES RATHER TO PROCESSES THAN TO STATES

NO DIRECT WM CONNECTIVITY MEASUREMENT

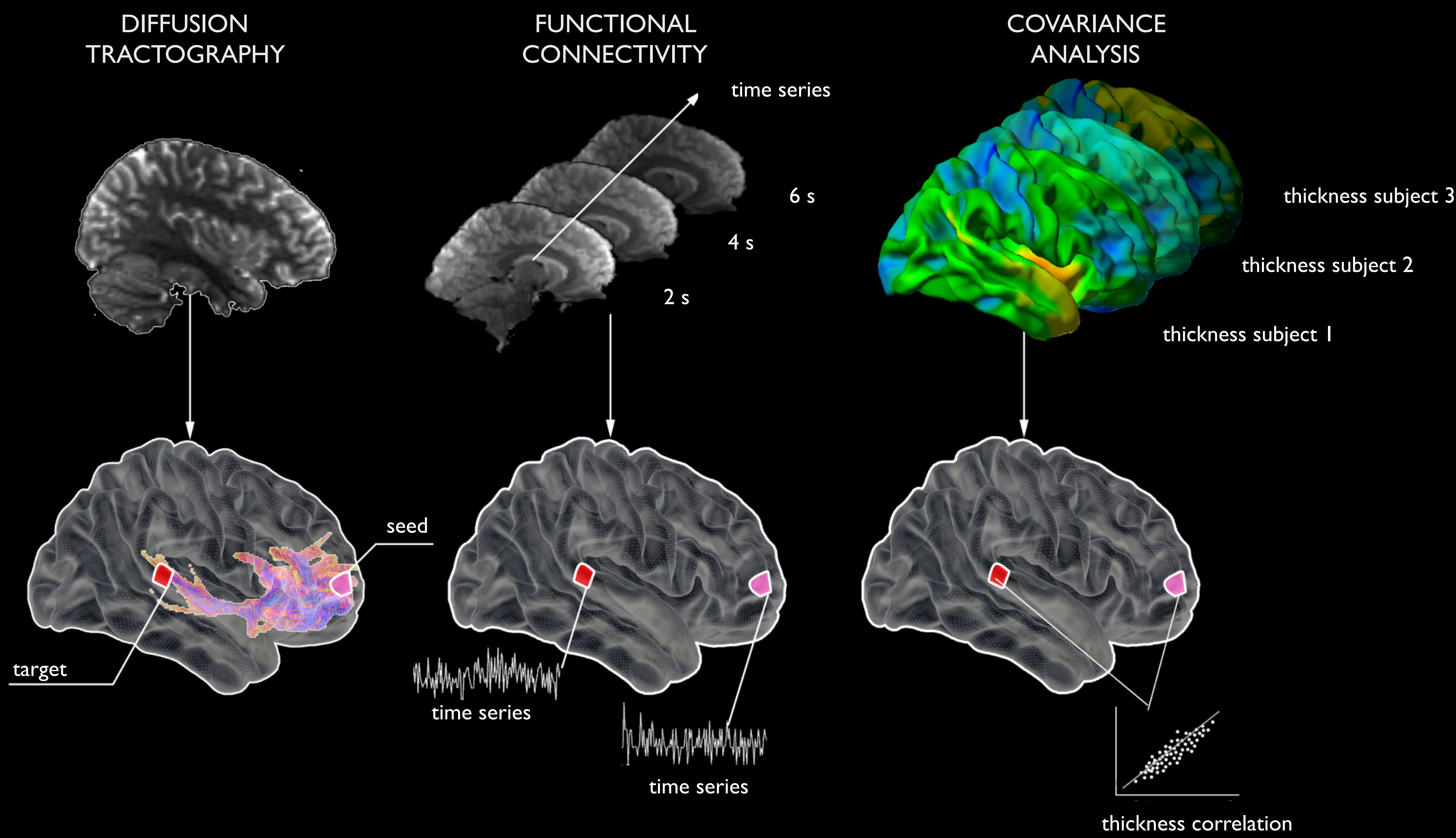




Alexander-Bloch, Bullmore, Giedd (2013) JNeurosci

HOW TO GENERATE CONNECTOMES

INTER-REGIONAL CONNECTIVITY ANALYSIS

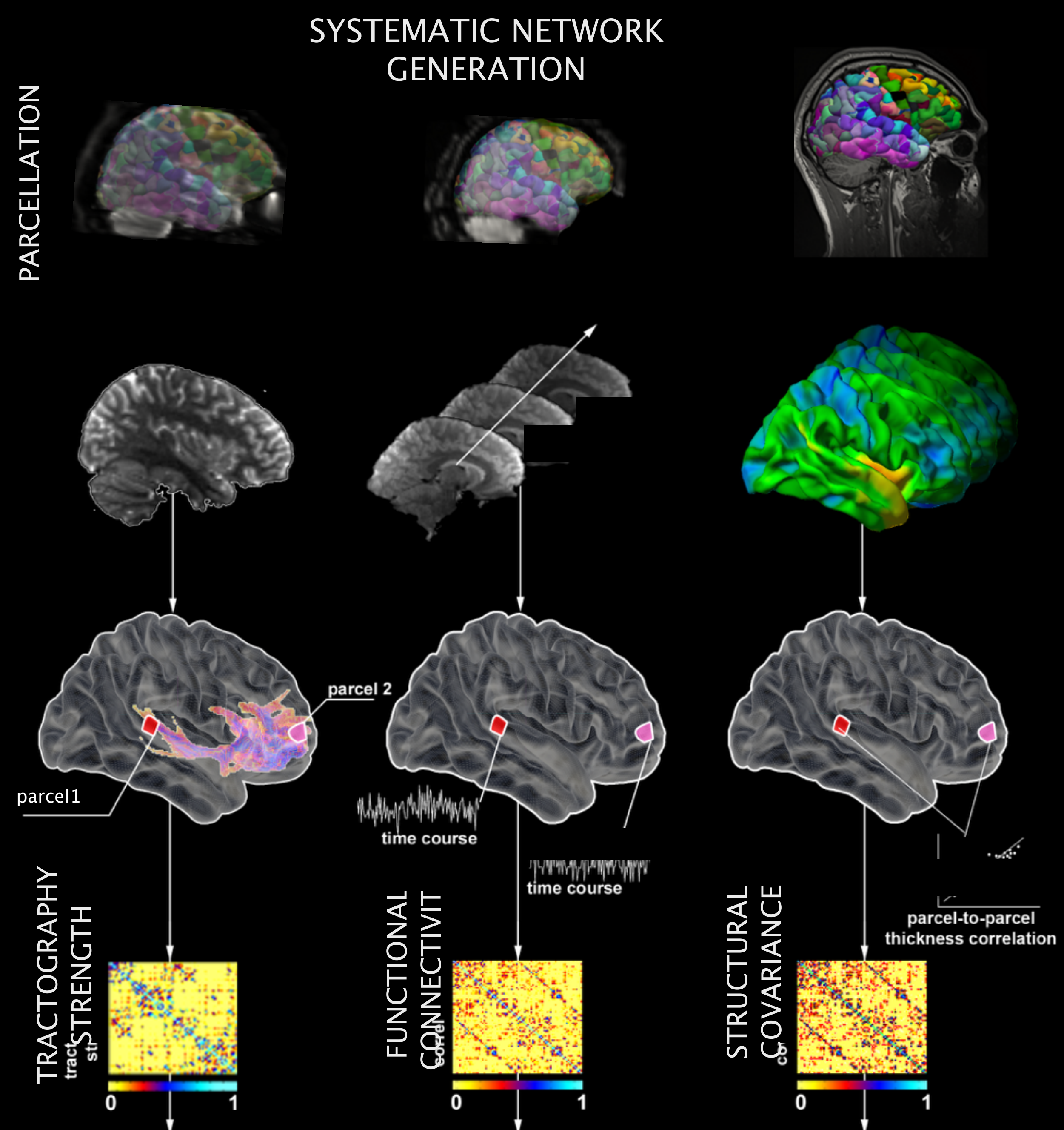


Mori et al. (1999) Ann Neu
Behrens et al. (2007) NIMG

Friston (1994) HBM
Smith (2012) NIMG

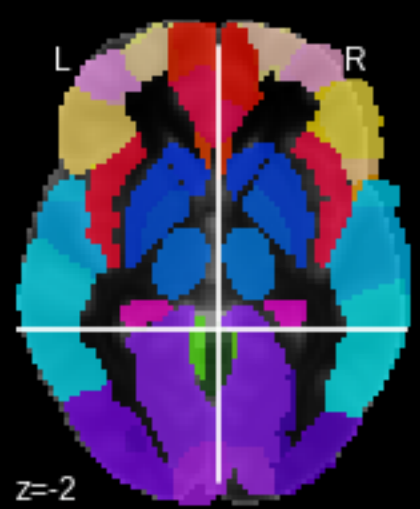
Lerch et al. (2006) NIMG
Alexander-Bloch et al. (2013) NRN

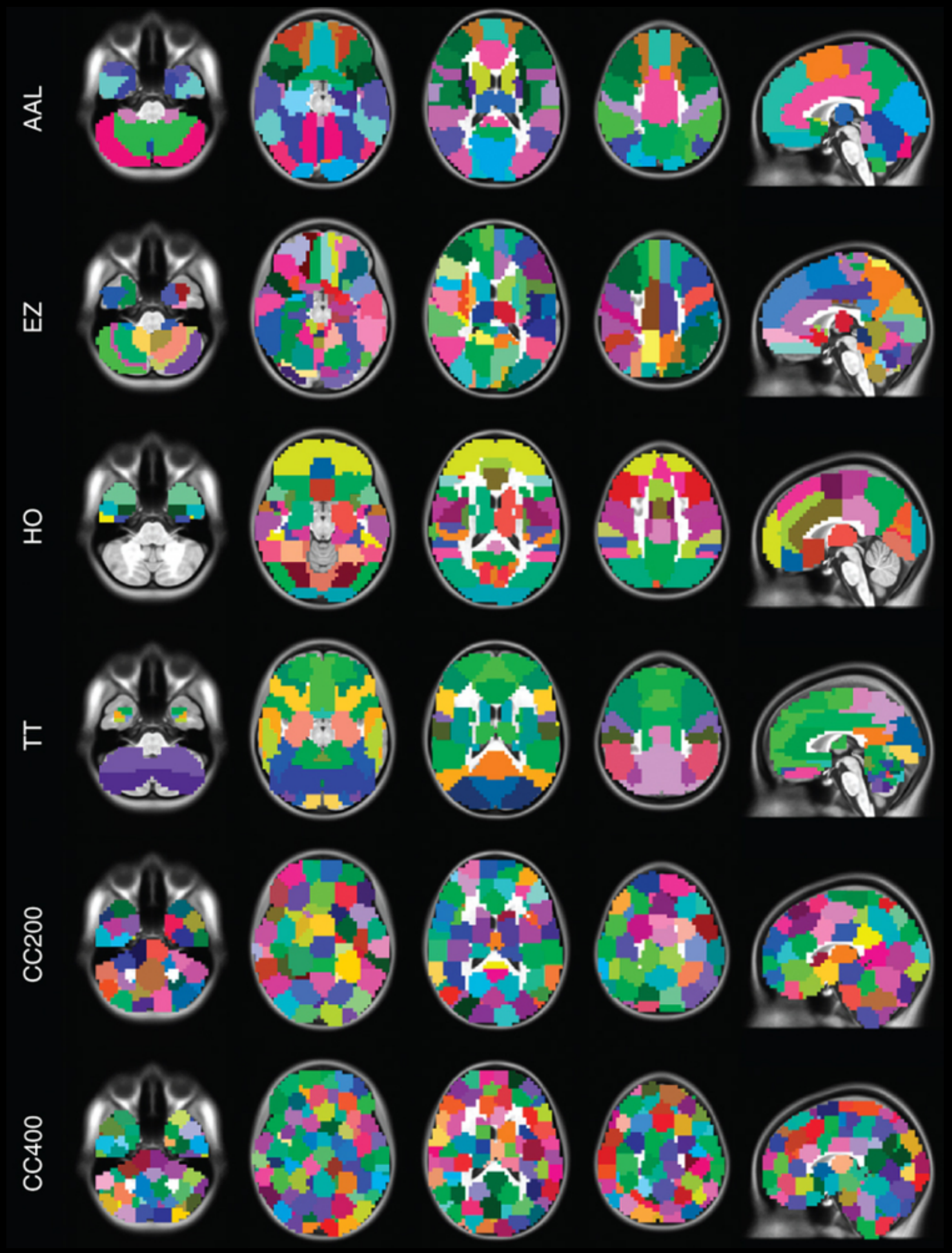
CONNECTOME ANALYSIS

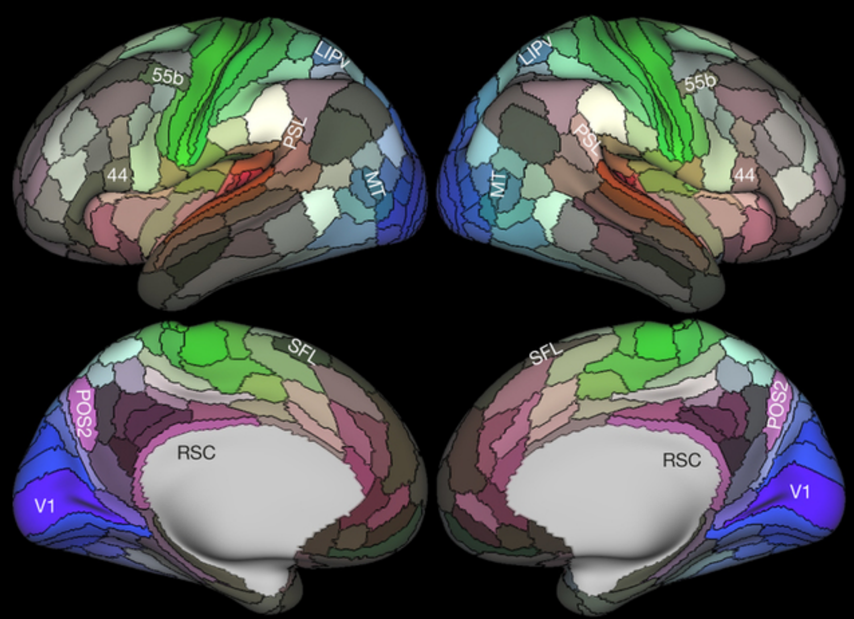


Bullmore and Sporns (2009) NRN, Watts and Strogatz (1998) Nature

DEFINITION OF REGION







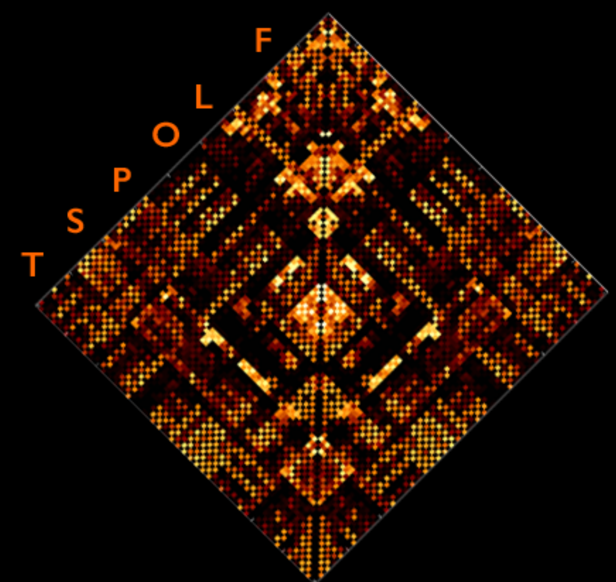
Tzuorio-Mazoyer et al (2002) Neuroimage

Craddock et al (2013) Nature Methods

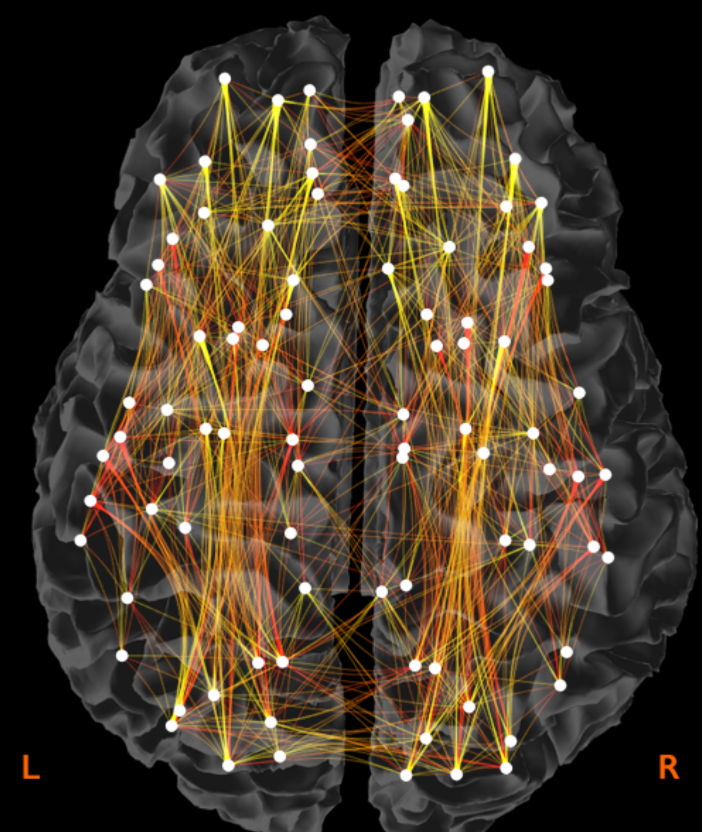
Glasser et al (2016) Nature

WHAT ASPECTS OF NETWORKS CAN BE MEASURED?

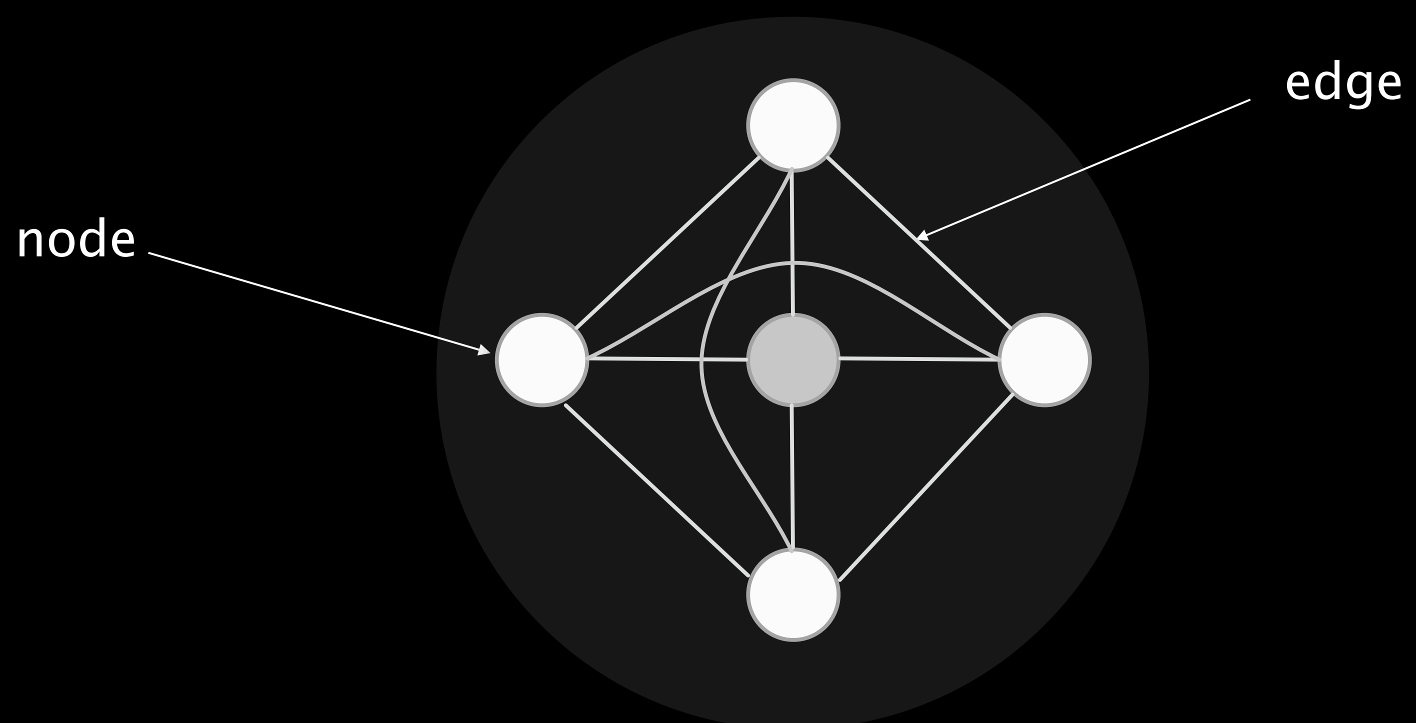
MATRICES AND GRAPHS



CONTROLS

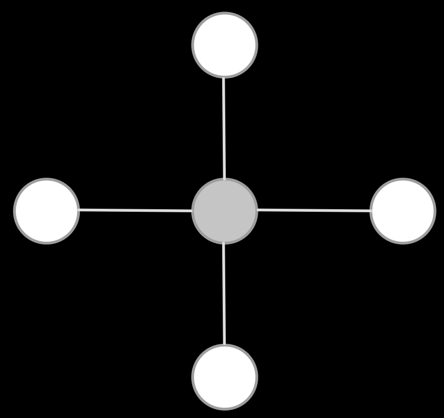


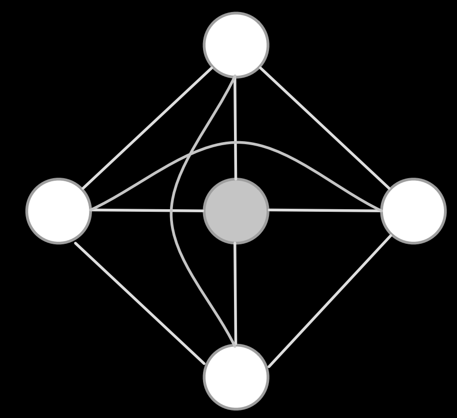
TOPOLOGY



τόπος, *place*, and λόγος, *study*

CLUSTERING COEFFICIENT C / gamma





low C

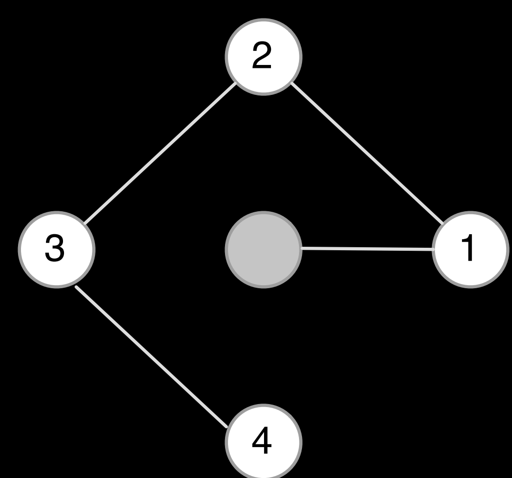
low local efficiency

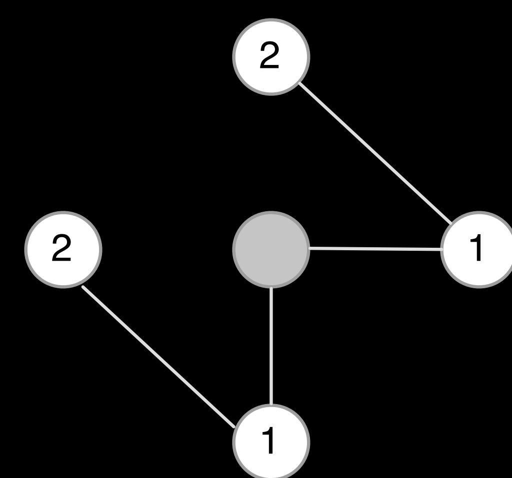
high C

high local efficiency

$$c_i = \frac{E_i}{\frac{k_i(k_i - 1)}{2}}.$$

PATH LENGTH P / Lambda





HIGH P

low global efficiency

LOW P

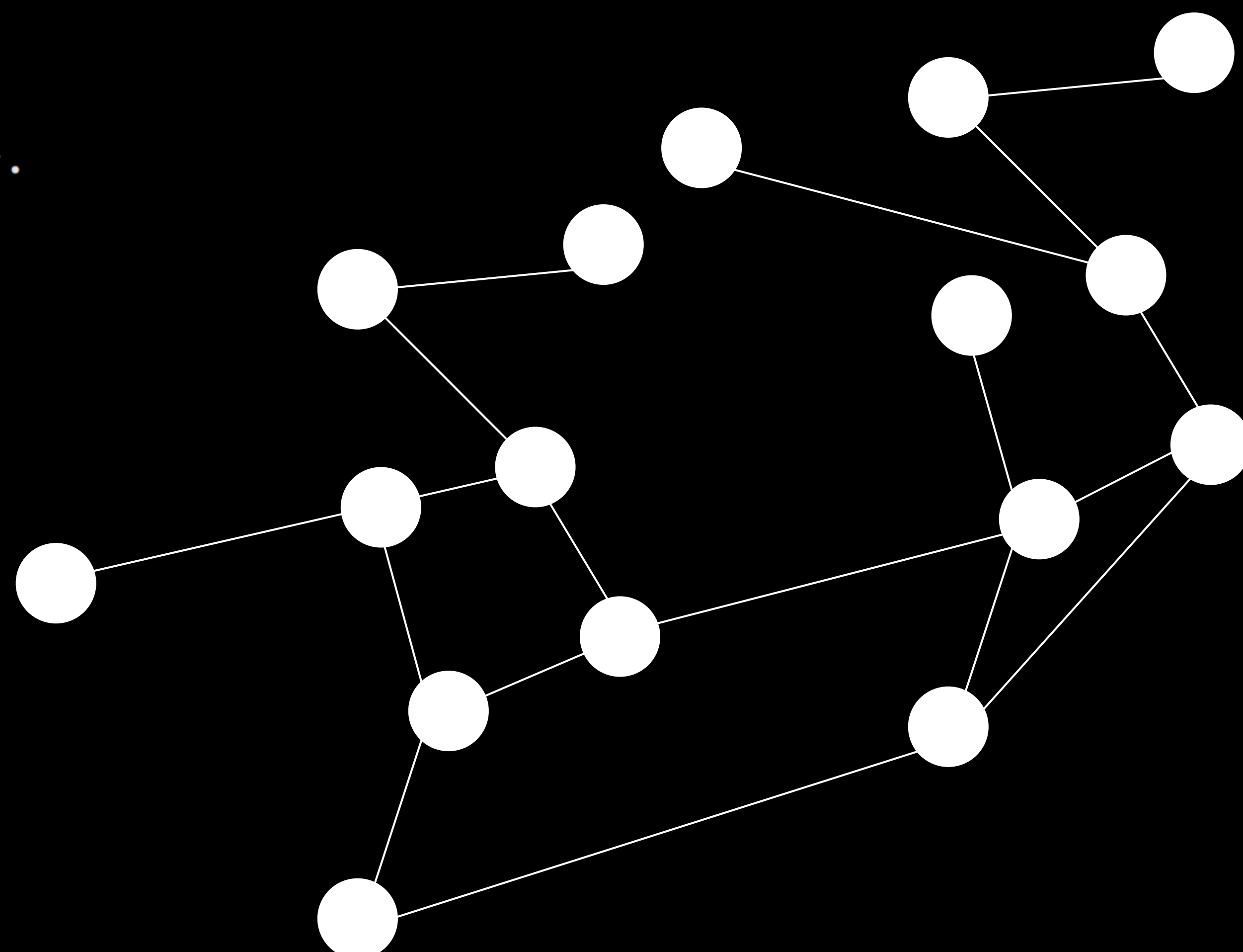
high global efficiency

$$l_i = \frac{1}{n-1} \sum_{i \neq j} \min\{ l_{ij} \}.$$

FROM NODES TO NETWORKS

$$l_i = \frac{1}{n-1} \sum_{i \neq j} \min\{ l_{ij} \}.$$

$$c_i = \frac{E_i}{\frac{k_i(k_i-1)}{2}}.$$

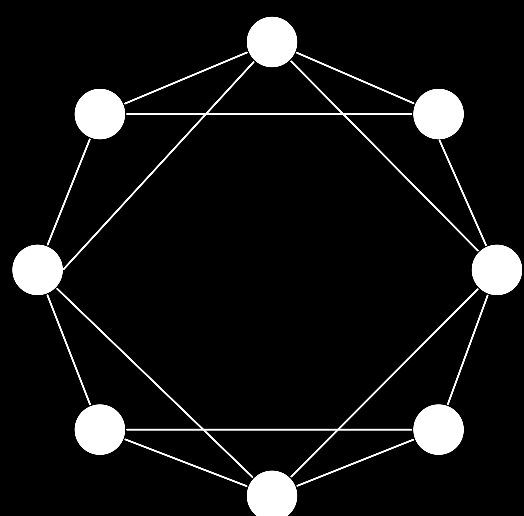


$$L = \frac{n}{\sum_{i=1}^{n} \frac{1}{li}}.$$

$$C = \frac{1}{n} \sum_{i=1}^{n} c_i.$$

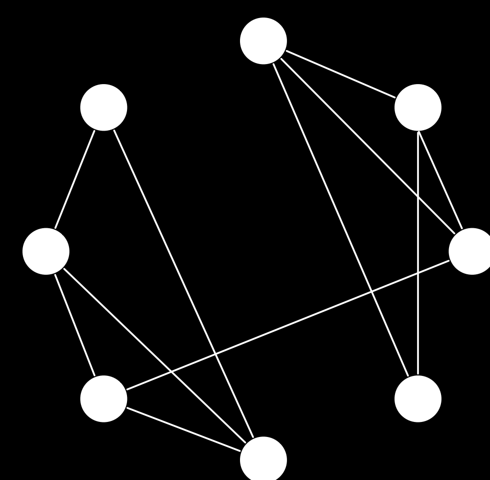
GLOBAL TOPOLOGY

REGULAR



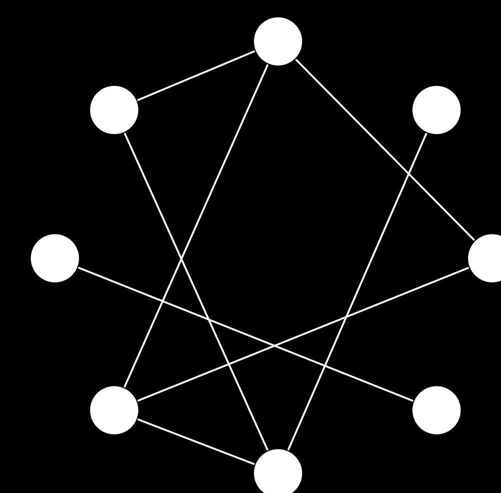
HIGH C
HIGH P

SMALL-WORLD



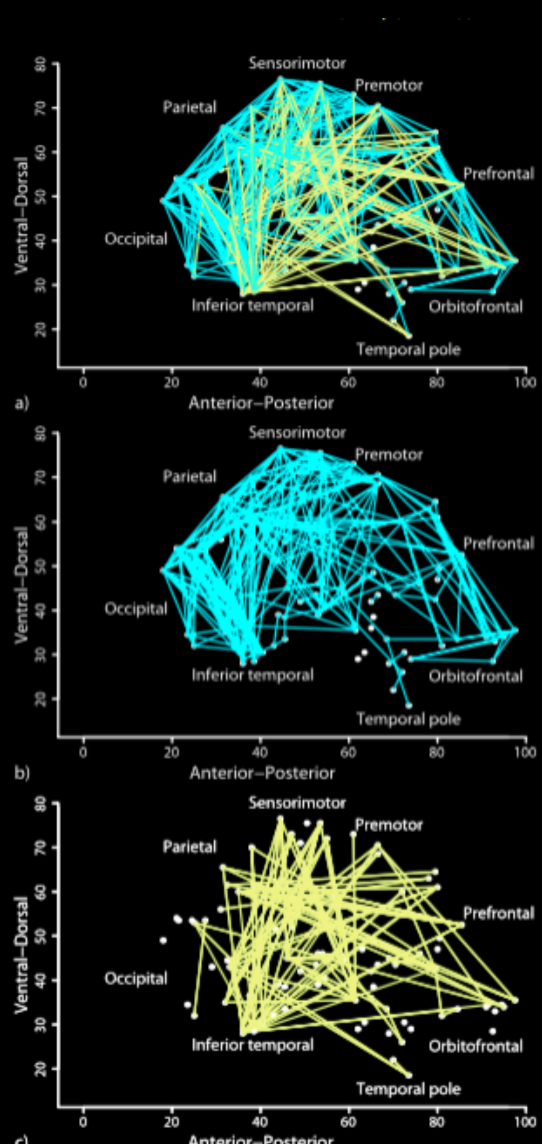
HIGH C
LOW P

RANDOM



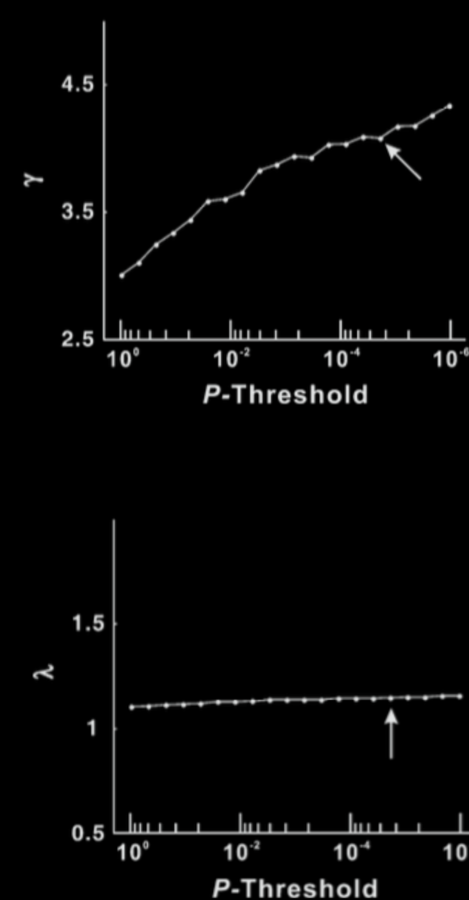
LOW C
LOW P

GLOBAL TOPOLOGY



$\theta = \gamma / \lambda > 1$

Archard et al (2006) JNeurosci



$\theta = \gamma / \lambda > 1$

Gong et al (2008) JNeurosci

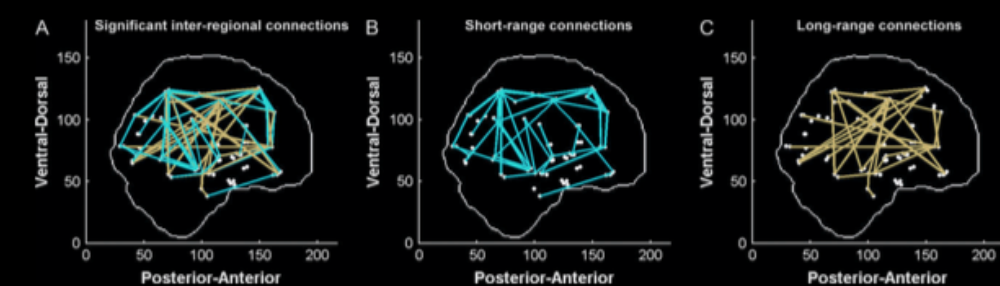
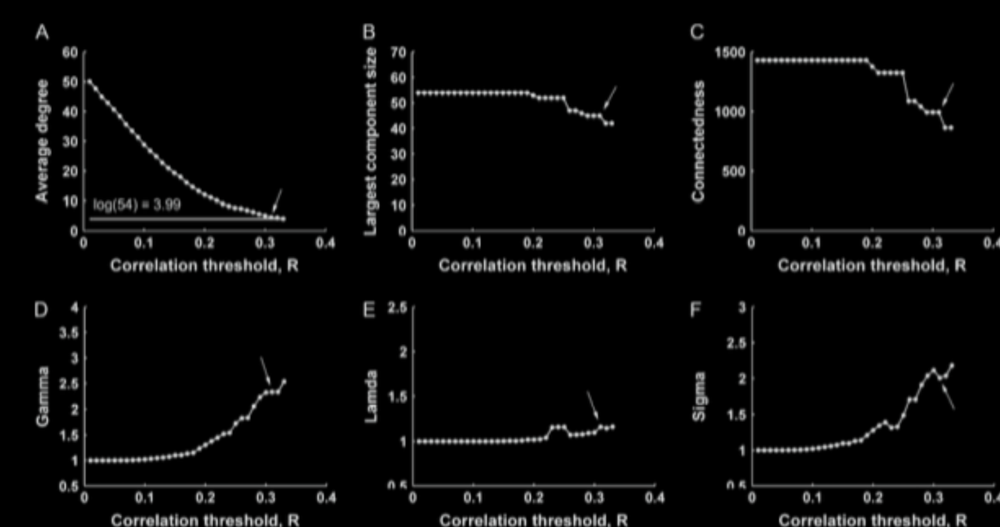


Figure 3. Short- and long-range anatomical connections in the anatomical space. (*A*) One hundred and four undirected edges (~7.3% of the 1431 possible connections among regions) representing the significant connections were shown in a sagittal view of the brain. Edges were classified into (*B*) short-range connections (D < 75 mm, red) and (*C*) long-range connections (D > 75 mm, blue) The locations of the nodes indicated the y and z coordinates of the regional centroids in Talairach space.



$\theta = \gamma / \lambda > 1$

He et al (2008) Cerebral Cortex

INTERMEDIATE TOPOLOGY: MODULARITY

Modularity and community structure in networks

M. E. J. Newman*

Department of Physics and Center for the Study of Complex Systems, University of Michigan, Ann Arbor, MI 48109

Edited by Brian Skyrms, University of California, Irvine, CA, and approved April 19, 2006 (received for review February 26, 2006)

Many networks of interest in the sciences, including social networks, computer networks, and metabolic and regulatory networks, are found to divide naturally into communities or modules. The problem of detecting and characterizing this community structure is one of the outstanding issues in the study of networked systems. One highly effective approach is the optimization of the quality function known as ''modularity'' over the possible divisions of a network. Here I show that the modularity can be expressed in terms of the eigenvectors of a characteristic matrix for the network, which I call the modularity matrix, and that this expression leads to a spectral algorithm for community detection that returns results of demonstrably higher quality than competing methods in shorter running times. I illustrate the method with applications to several published network data sets.

clustering | partitioning | modules | metabolic network | social network

Many systems of scientific interest can be represented as networks, sets of nodes or vertices joined in pairs by lines or edges. Examples include the internet and the worldwide web, metabolic networks, food webs, neural networks, communication and distribution networks, and social networks. The study of

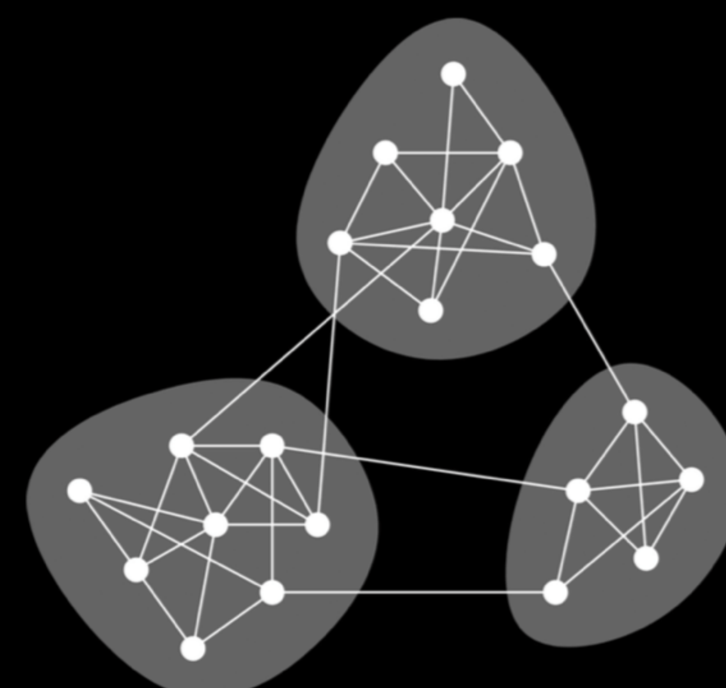
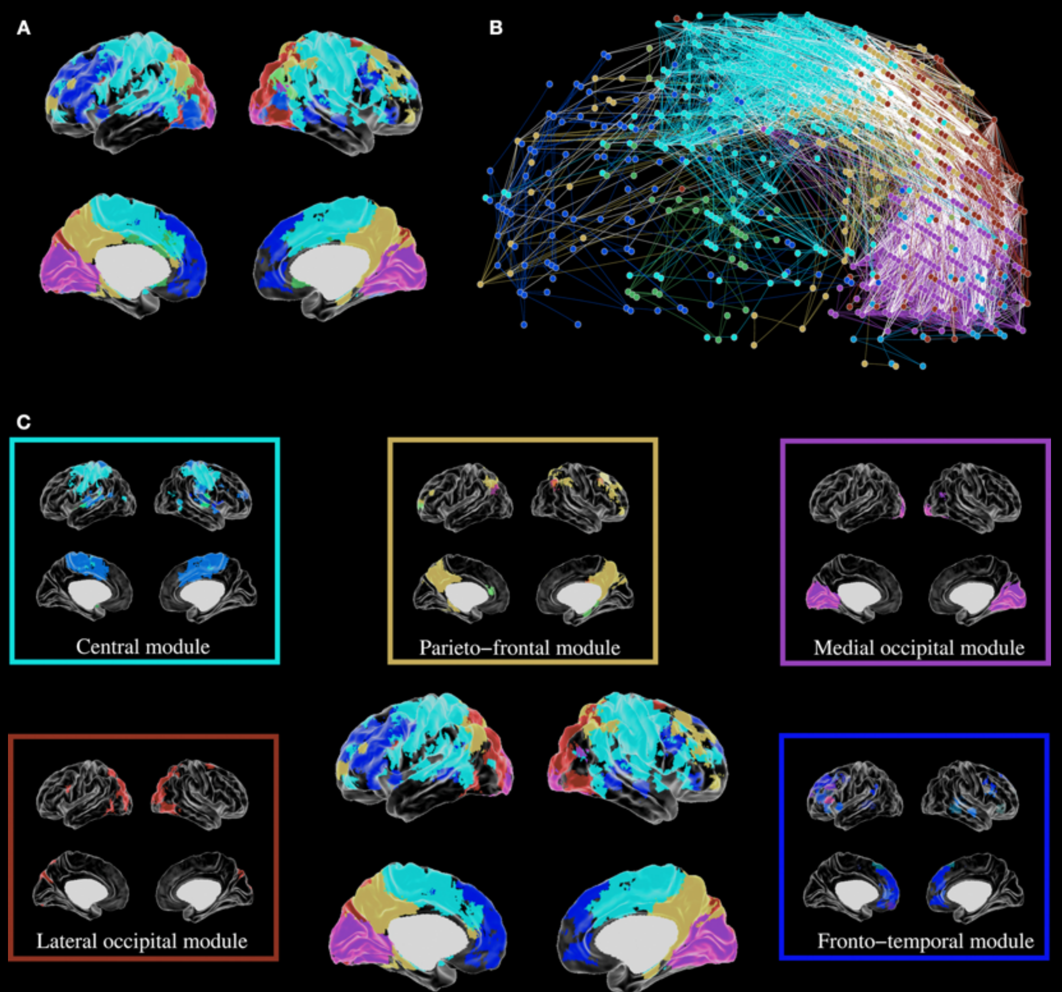
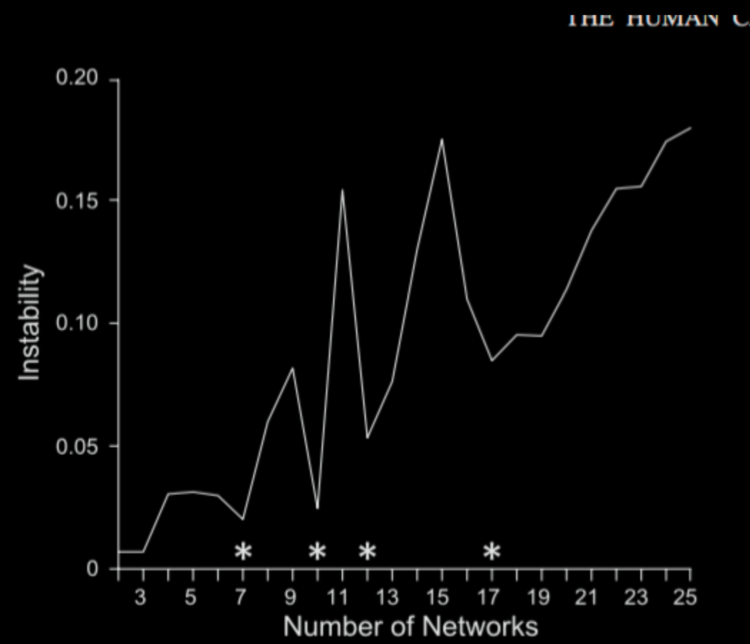


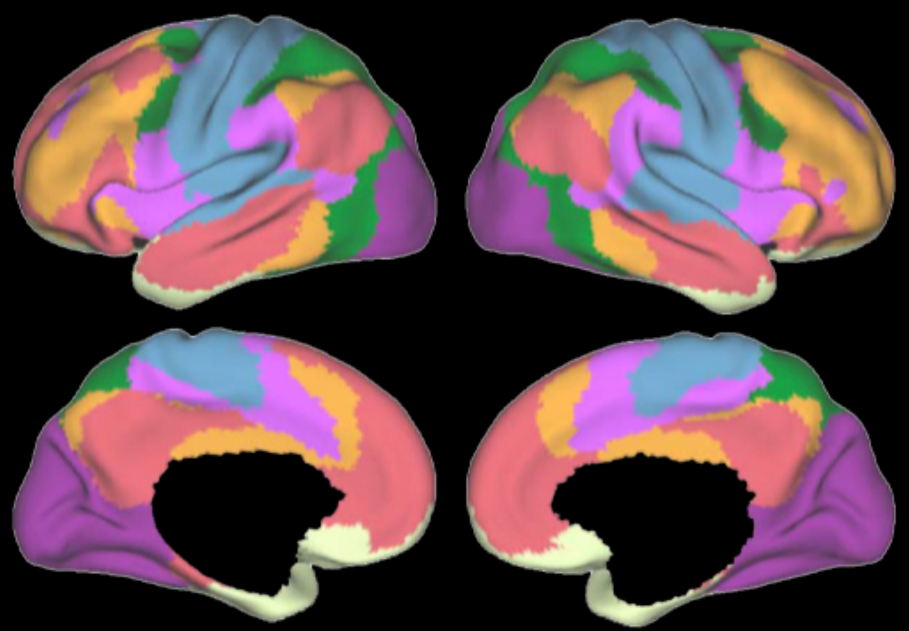
Fig. 1. The vertices in many networks fall naturally into groups or communities, sets of vertices (shaded) within which there are many edges, with only a smaller number of edges between vertices of different groups.

Newman (2006) PNAS

INTERMEDIATE TOPOLOGY: MODULARITY



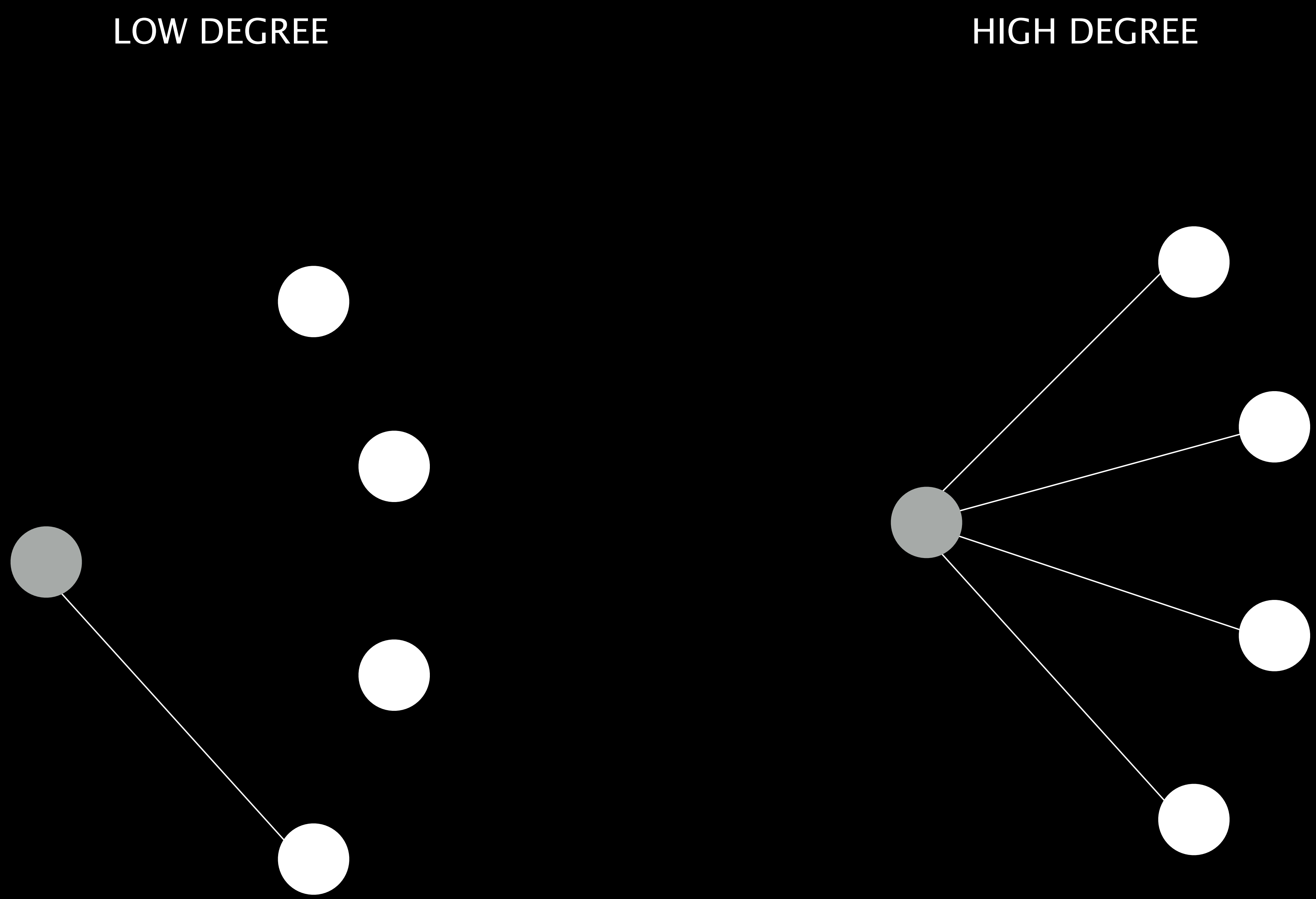




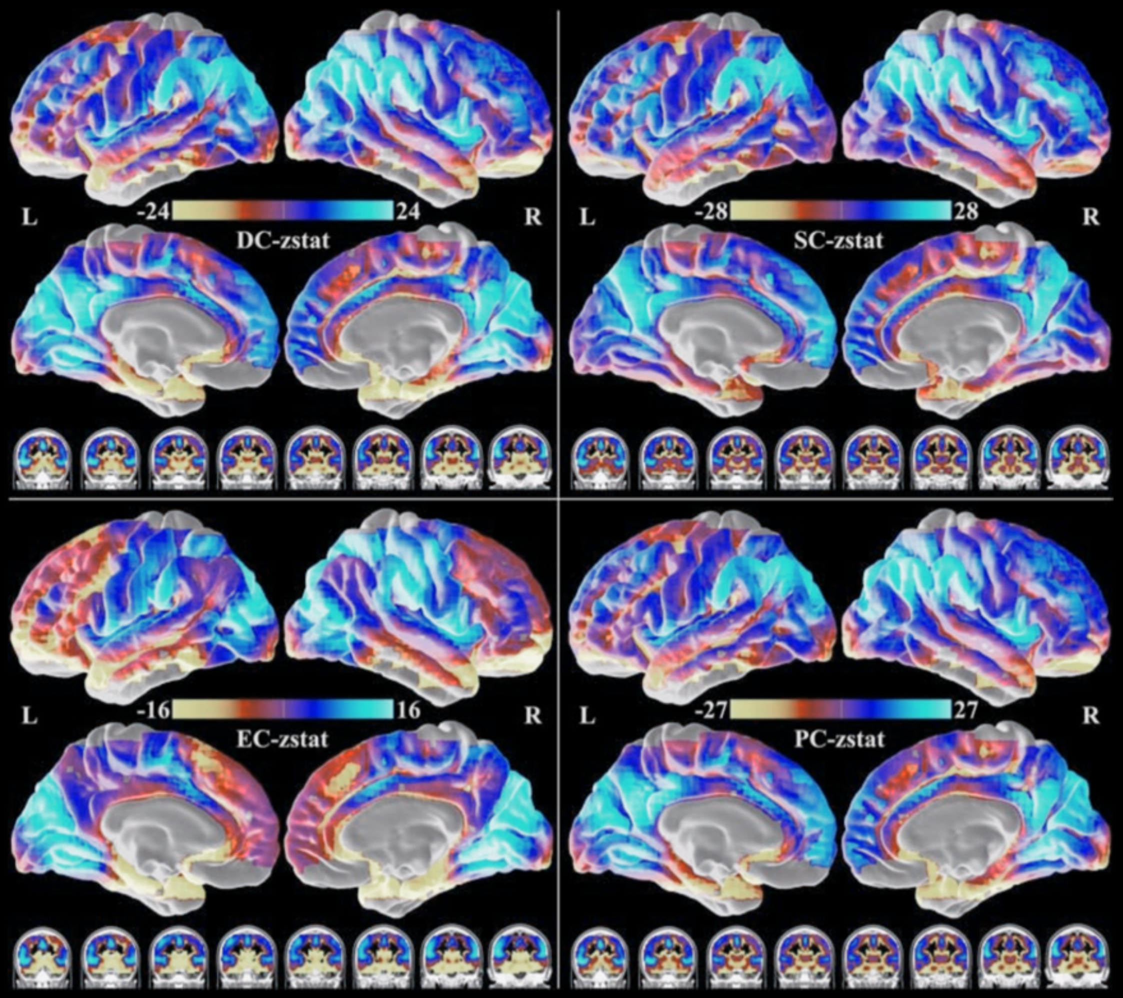
Meunier et al (2009) Front Neuroinf

Yeo, Krienen, et al (2011) JNeurophysiol

NODAL TOPOLOGY: CENTRALITY

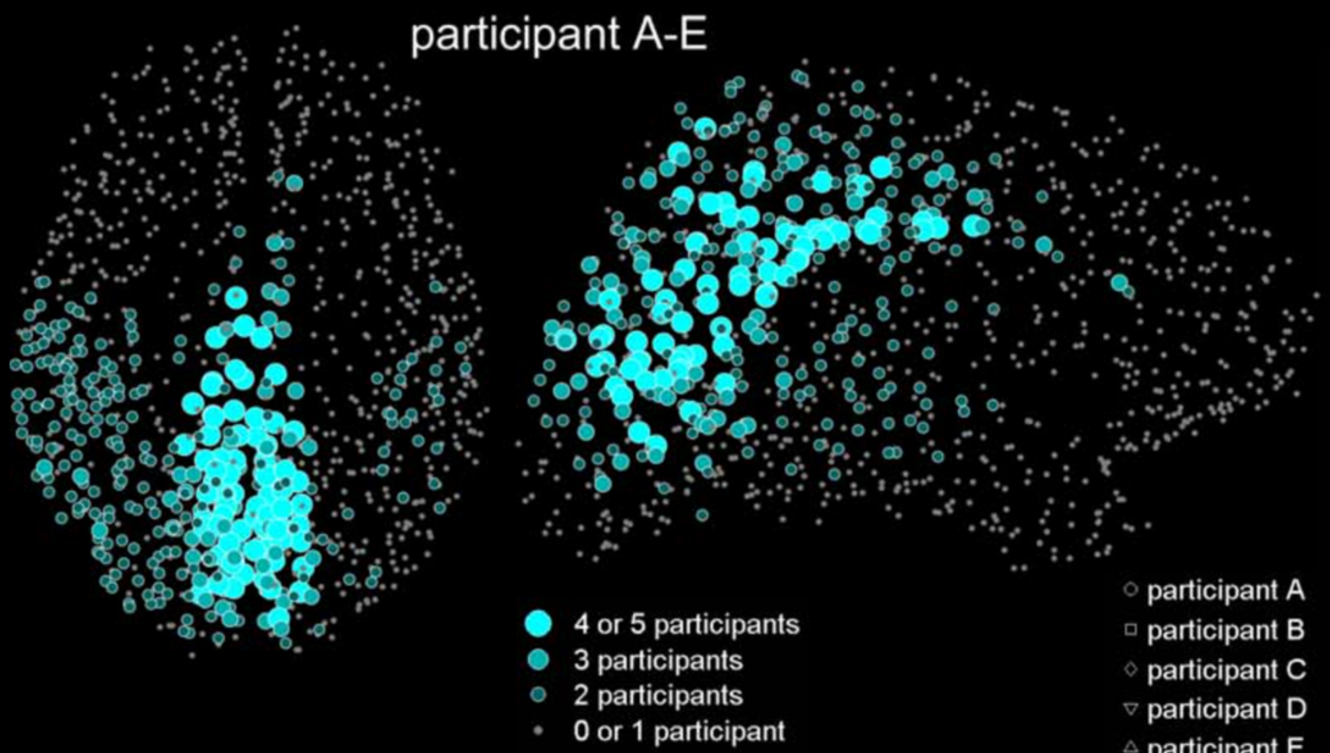


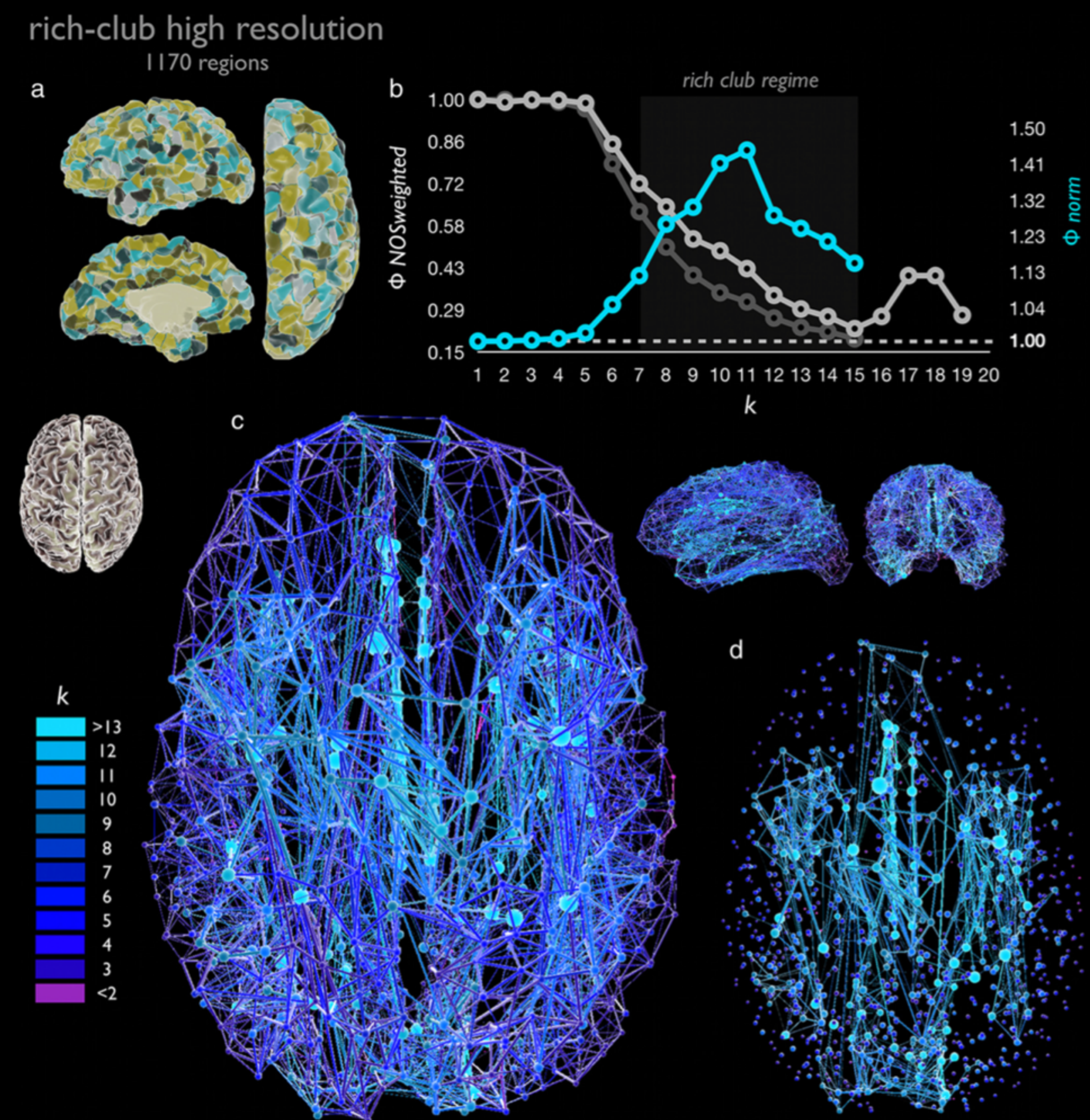
NODAL TOPOLOGY: CENTRALITY



Zuo et al (2014) Cerebral Cortex

NODAL TOPOLOGY: RICH-CLUB AND CORES





Hangman et al (2008) PloS Biol

Van den Heuvel and Sporns (2011) JN

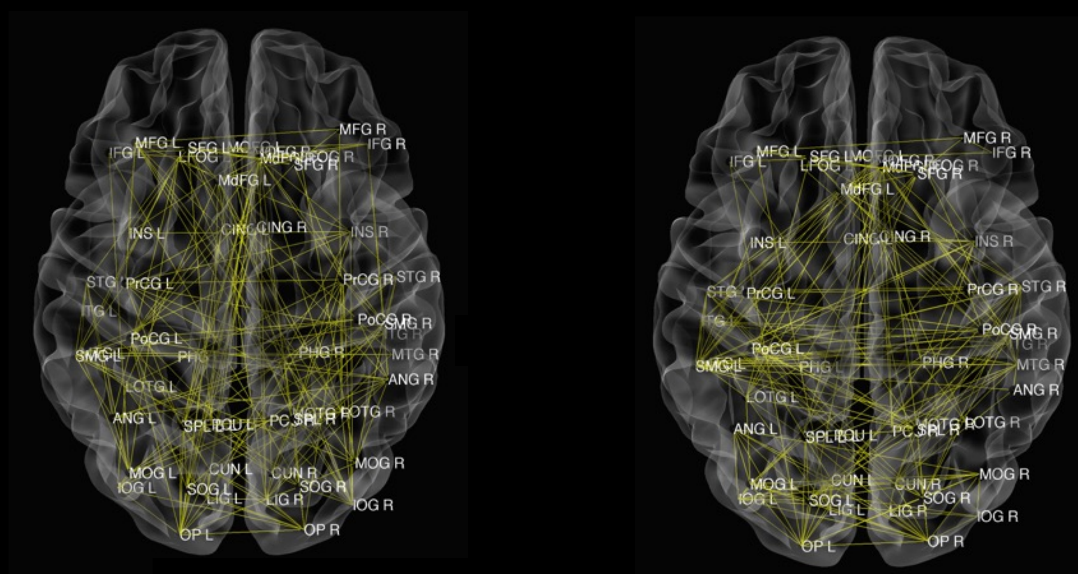
WHAT HAS BEEN SHOWN IN EPILEPSY?

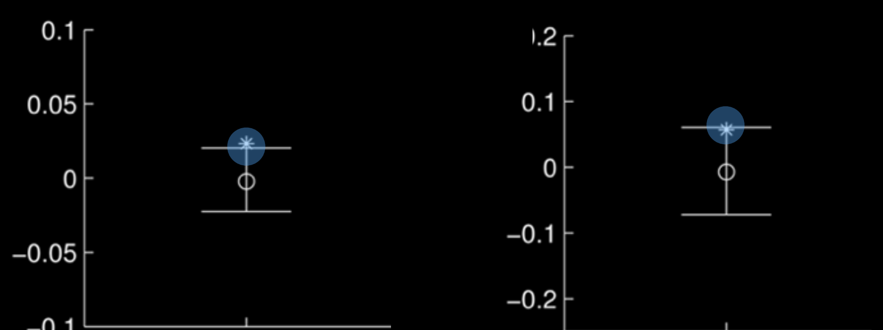
LARGE-SCALE CHANGES: STRUCTURAL COVARIANCE NETWORKS

NEOCORTEX

CONTROLS

TLE





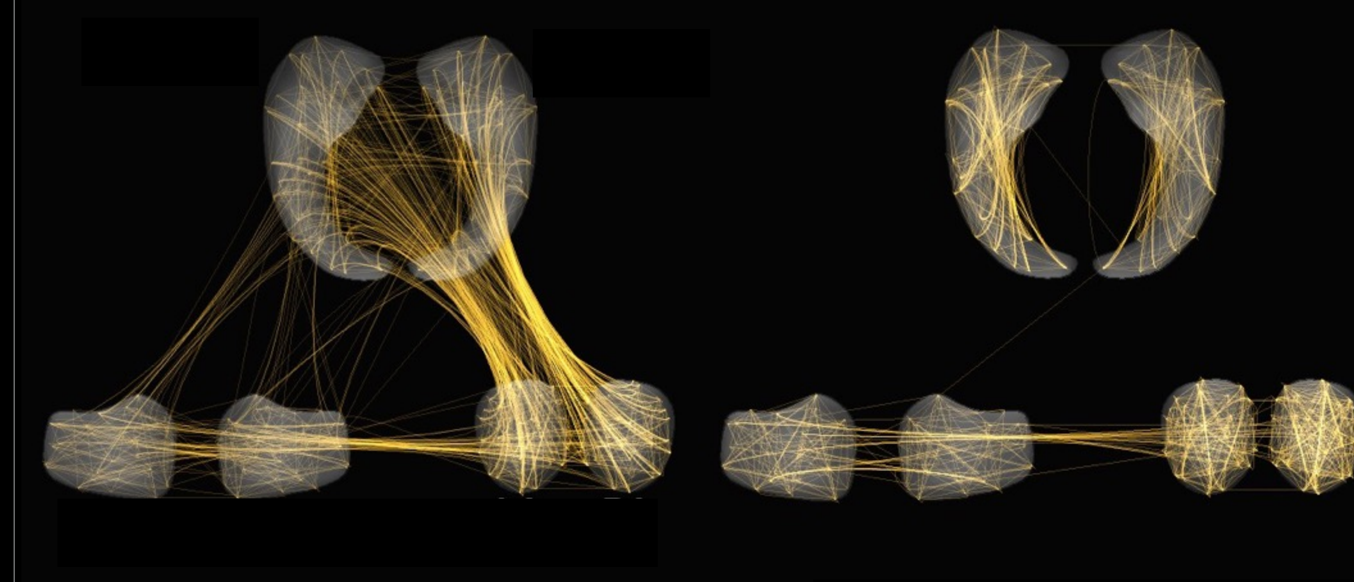
CLUSTERING

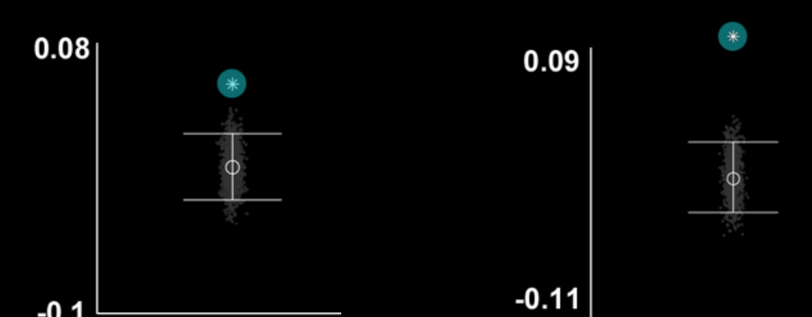
PATH LENGTH

MESIOTEMPORAL LOBE

CONTROLS

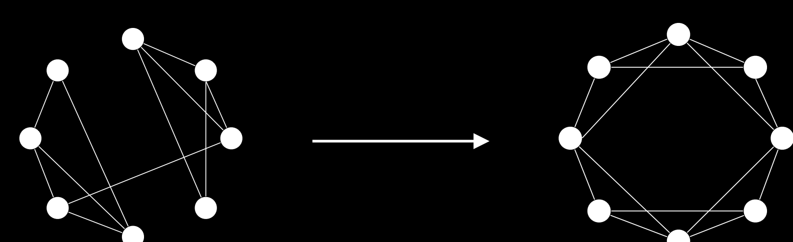
TLE





CLUSTERING

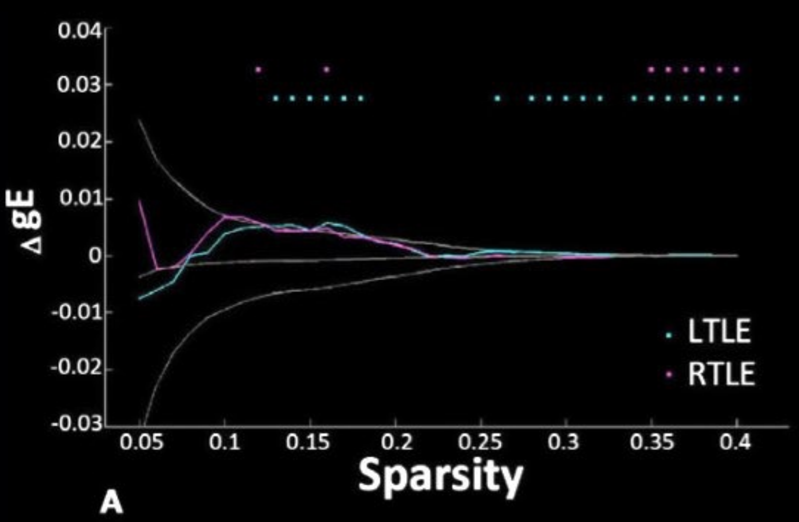
PATH LENGTH

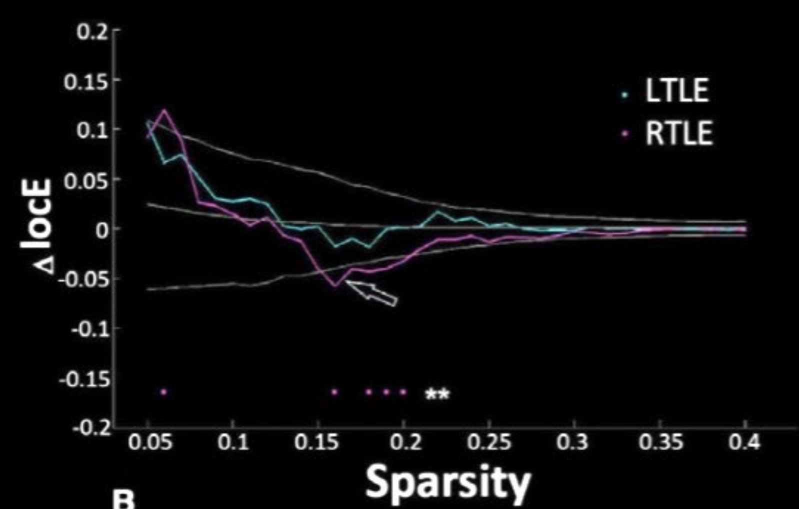


Bernhardt et al. (2011, 2016) Cerebral Cortex

LARGE-SCALE STRUCTURAL CHANGES

CORTICAL AND SUBCORTICAL VOLUME COVARIANCE





Yasuda et al. (2015) Epilepsia

DETERMINISTIC DIFFUSION TRACTOGRAPHY

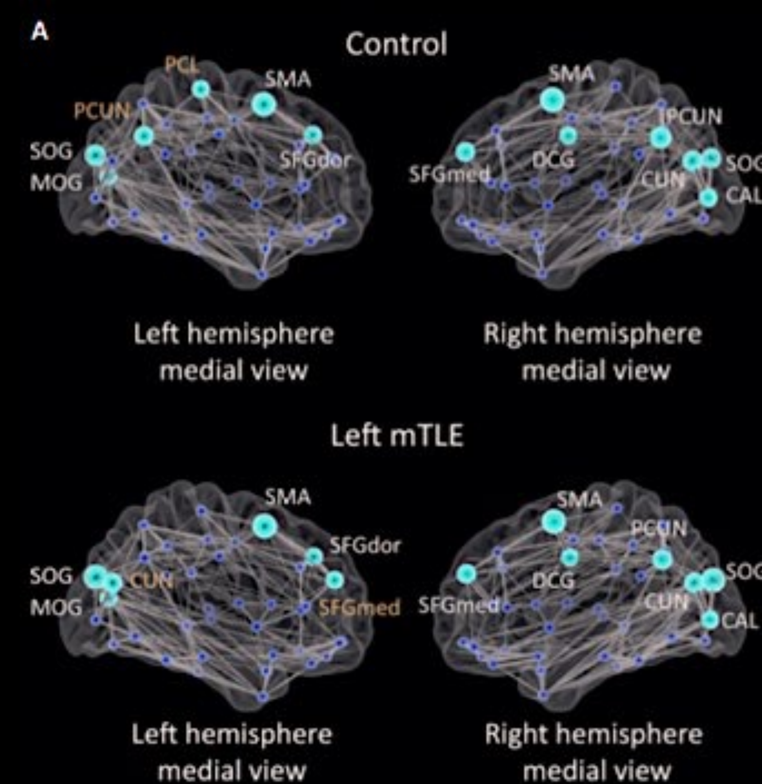


Table 2. Global network properties and between-group comparison results between patients with left mTLE and controls

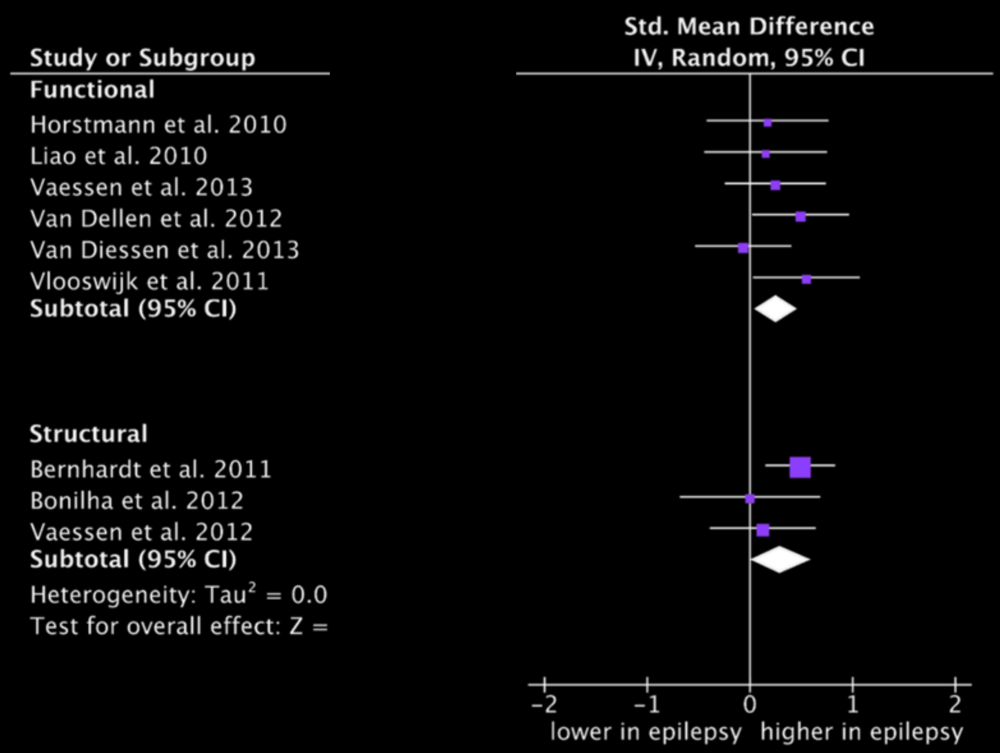
	left mTLE	Controls	T	p-Value
K	1,402 ± 124	1,547 ± 71	−4.27	<0.001[a]
S	0.18 ± 0.06	0.19 ± 0.03	−0.83	0.42
C	0.38 ± 0.02	0.38 ± 0.01	1.14	0.26
L	1.06 ± 0.10	0.97 ± 0.05	3.70	<0.001[a]
E_{glob}	0.95 ± 0.09	1.03 ± 0.06	−3.51	0.001[a]
E_{loc}	1.32 ± 0.08	1.41 ± 0.05	−3.69	<0.001[a]

[a]Significant p-value < 0.05.

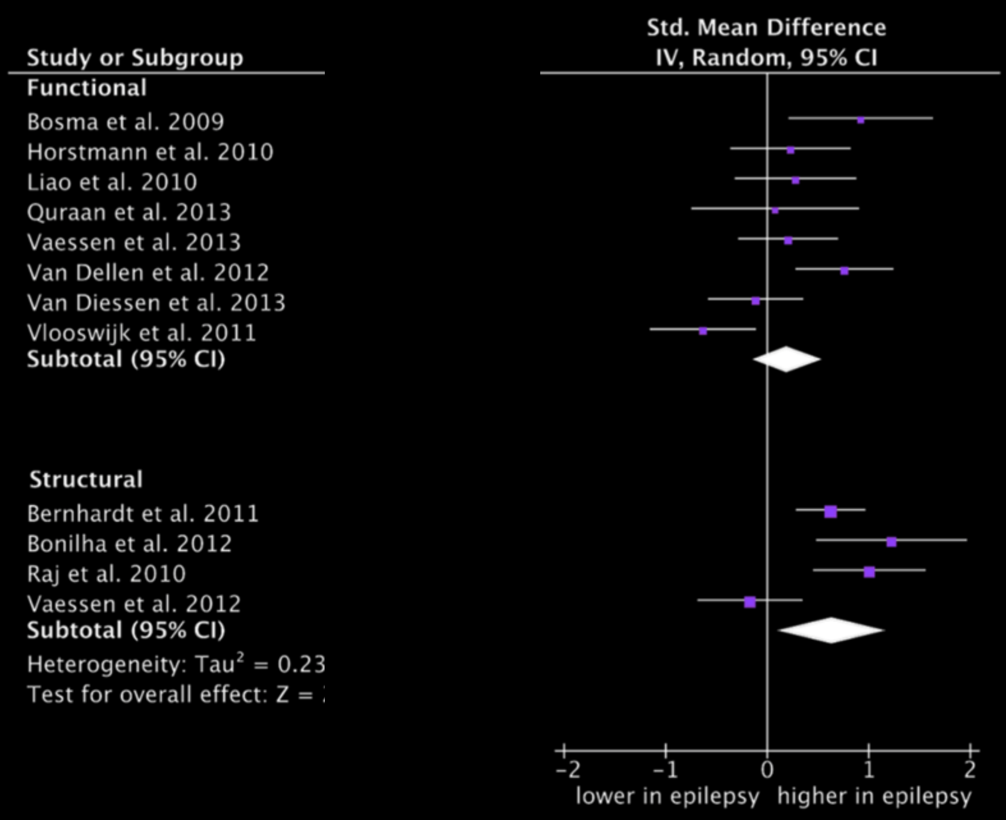
Liu et al. (2014) Epilepsia

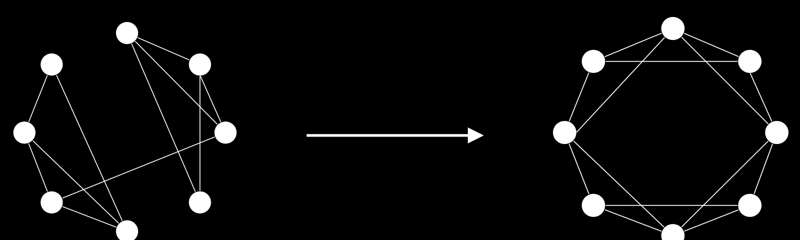
META-ANALYTICAL FINDINGS ON NETWORK TOPOLOGY

CLUSTERING COEFFICIENT



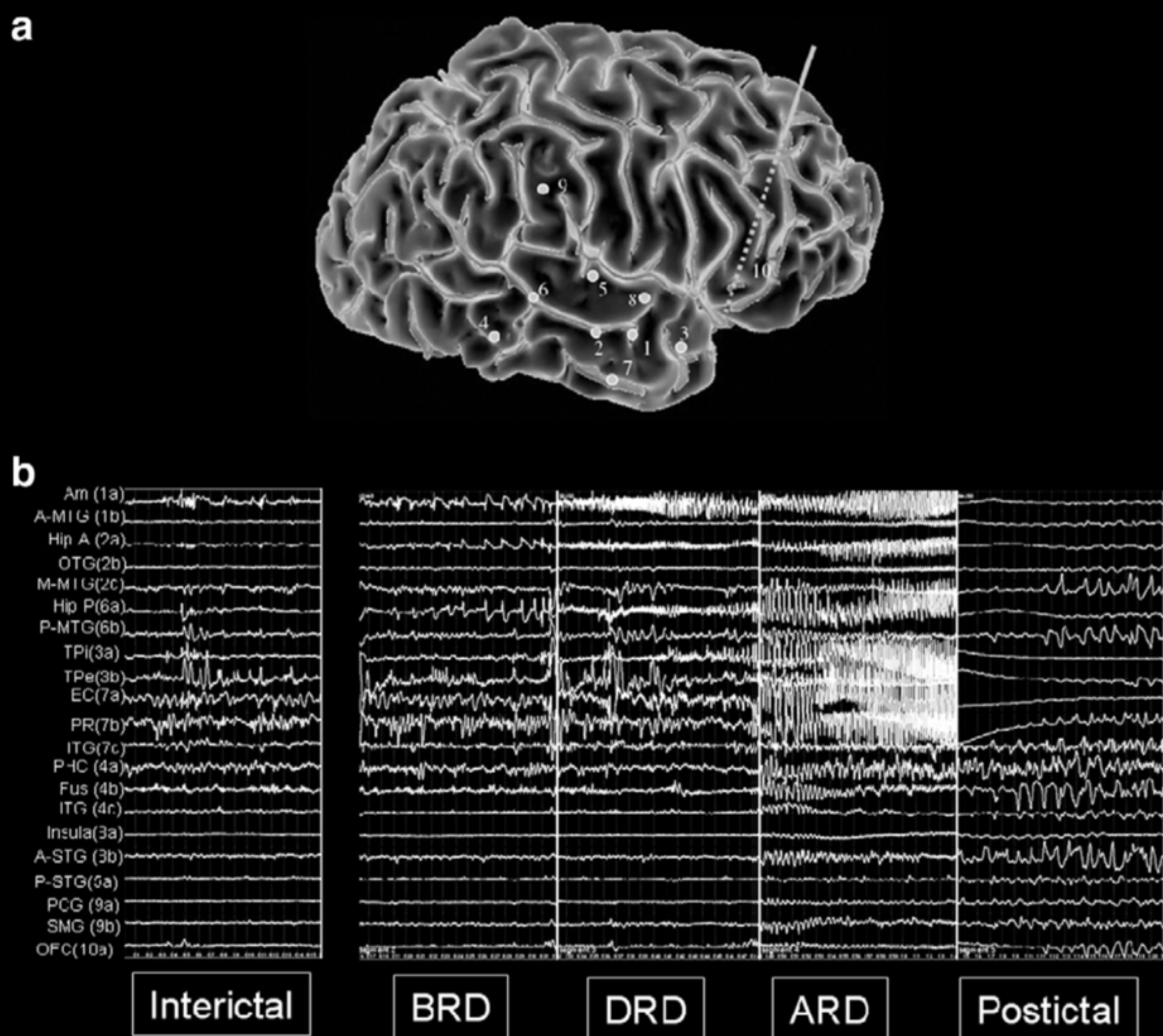
PATH LENGTH

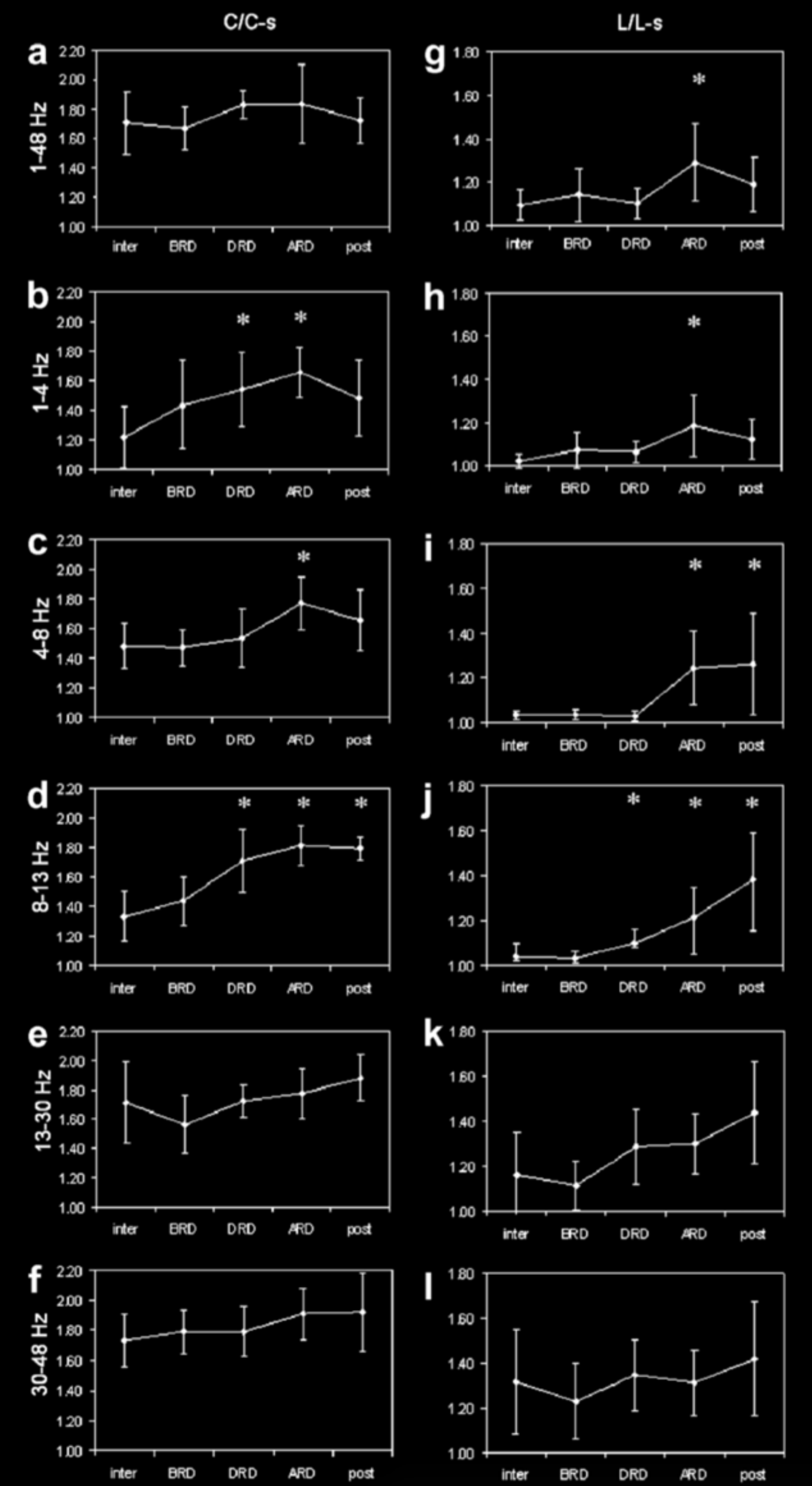




Van Diessen et al. (2014) PLoS One

REGULARIZATION ALSO SEEN DURING SEIZURES





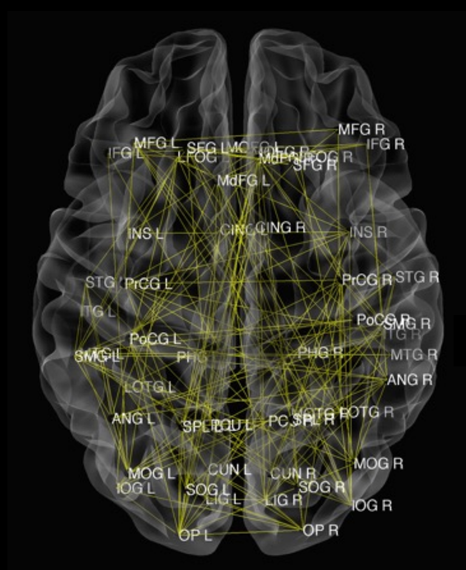
Ponten et al. (2009) Clin Neuropsy

CLINICAL APPLICATIONS BEYOND DESCRIPTION

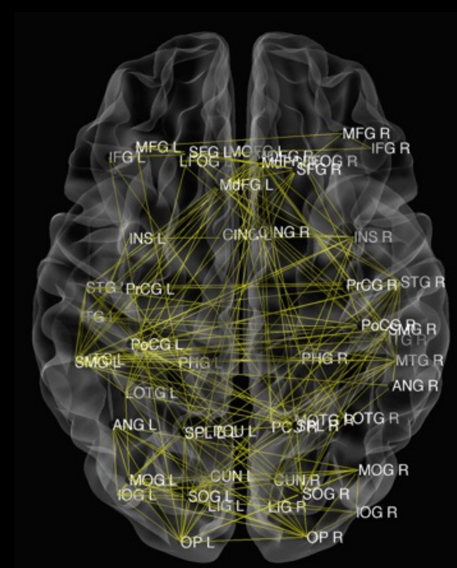
CLINICAL APPLICATIONS 1: PREDICTION OF OUTCOMES

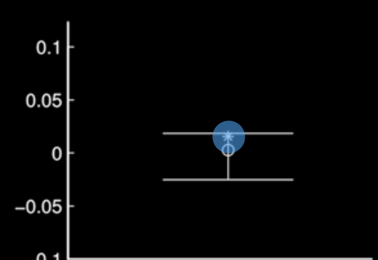
NEOCORTEX

CONTROLS

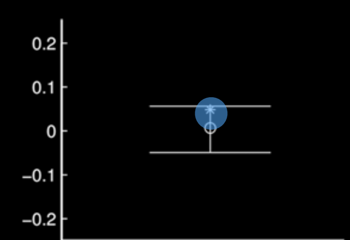


TLE





CLUSTERING



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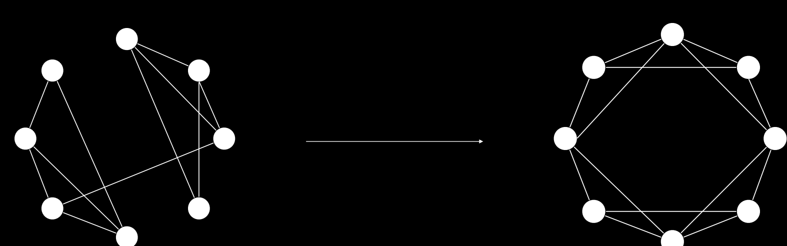

worse outcome

MESIOTEMPORAL LOBE

CONTROLS

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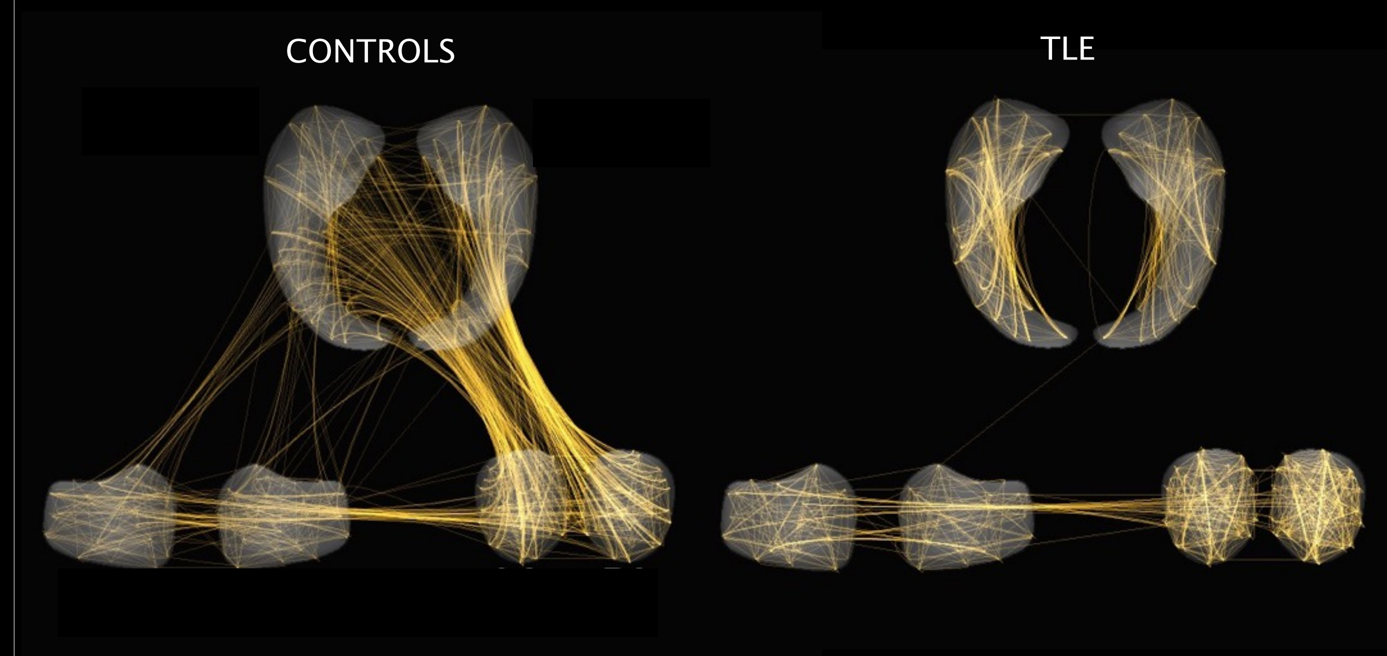

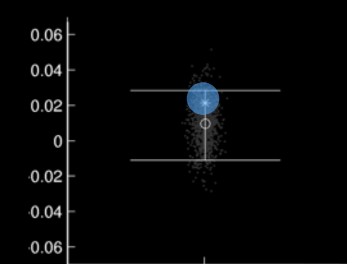

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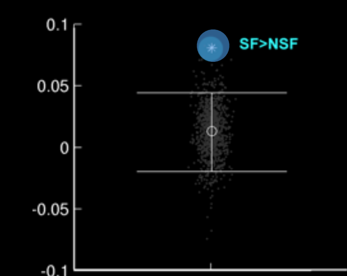

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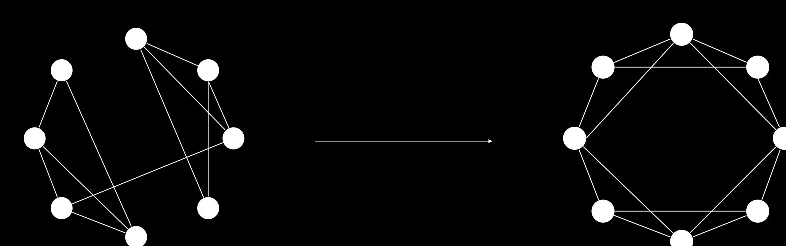
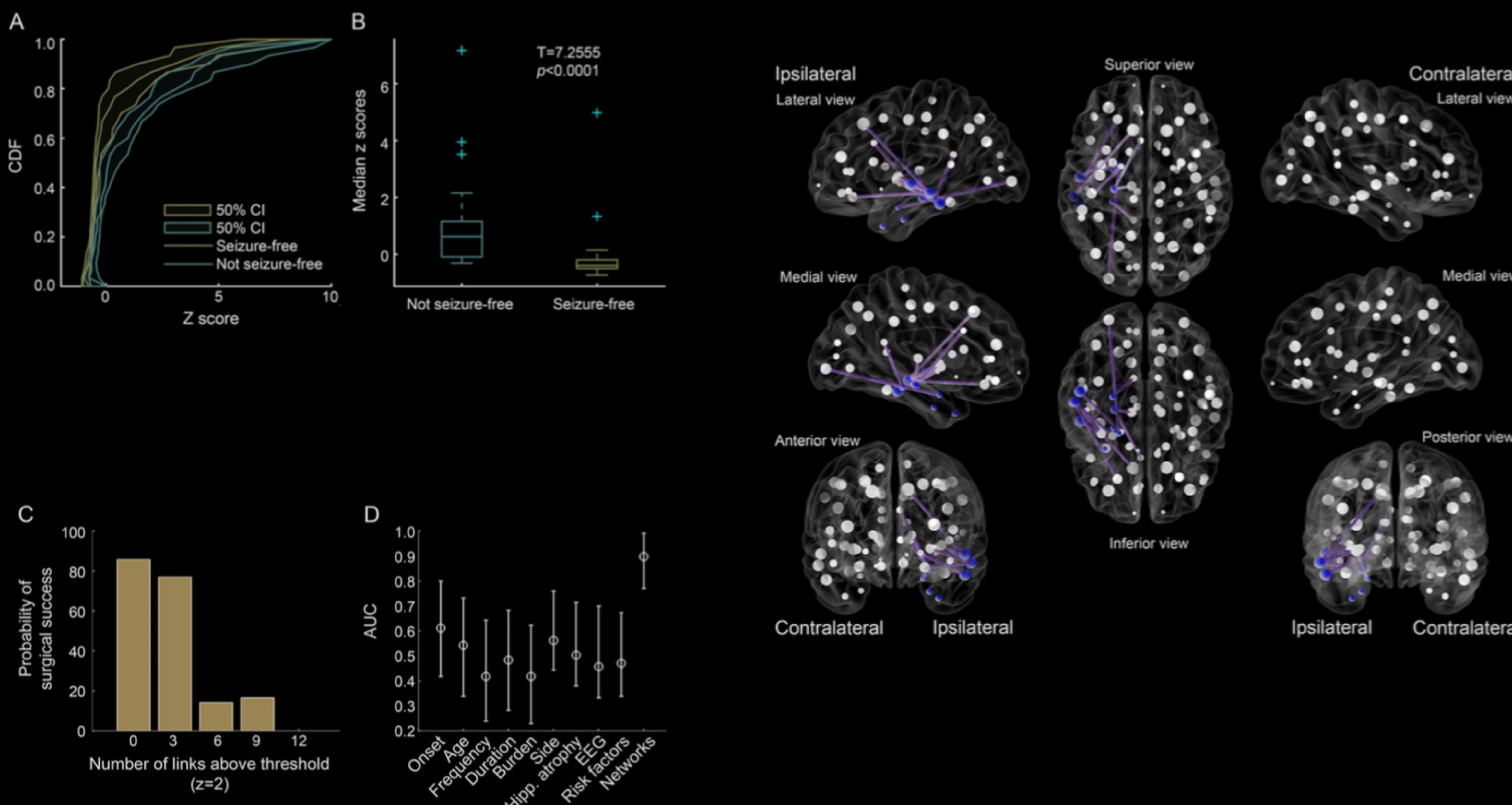


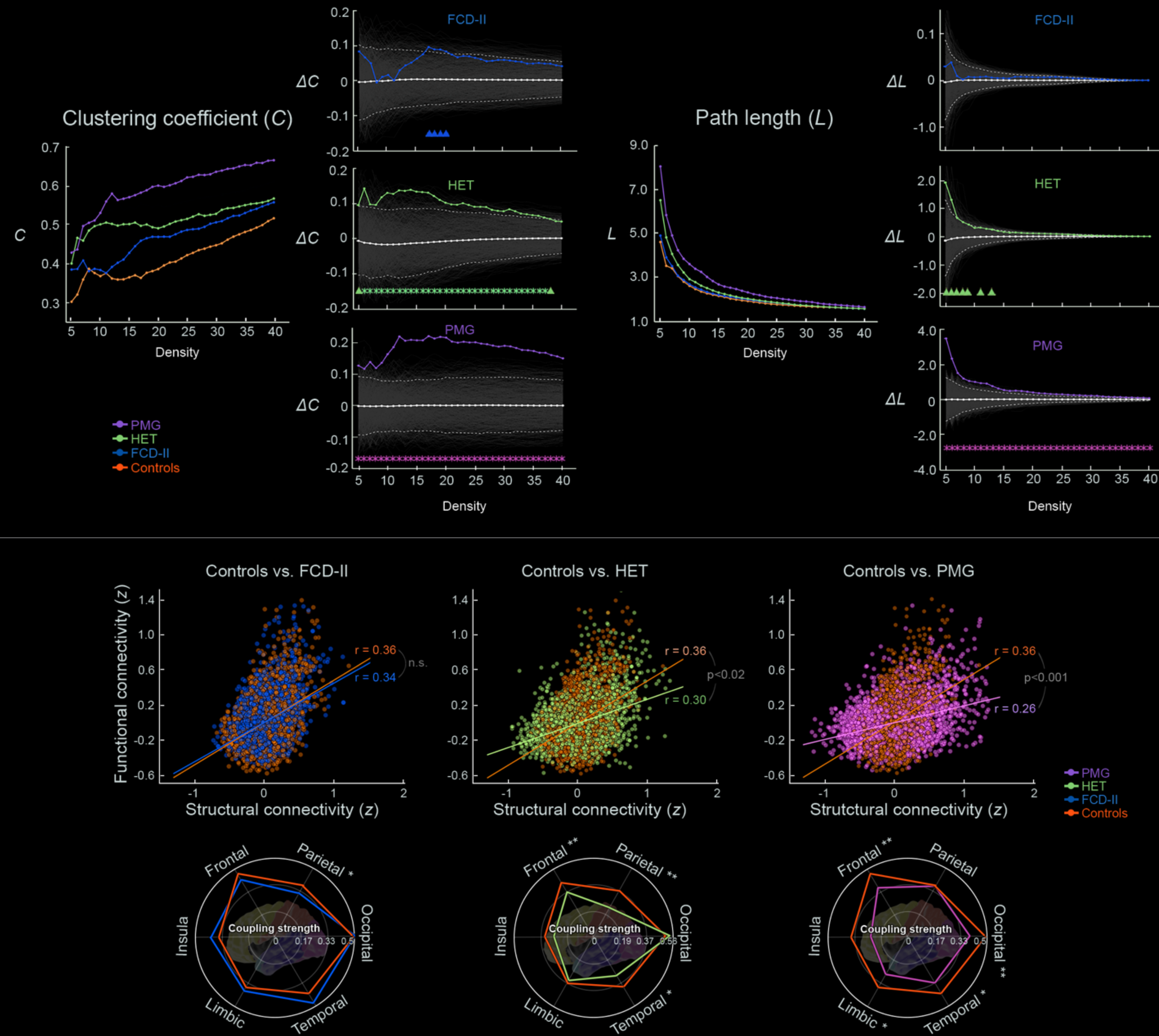
better outcome

CLINICAL APPLICATIONS 1: PREDICTION OF OUTCOMES



Bonilha et al. (2015) Neurology

BEYOND DESCRIPTION 2: STRUCTURE FUNCTION STUDIES



Hong, Bernhardt, et al. (2017) Brain

neuro

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