

FROM MICROSTRUCTURE TO MACROSCALE: NEUROIMAGING AND CONNECTOMICS IN HEALTHY AND DISEASED BRAINS

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THE POWER OF NEUROIMAGING

WIDELY AVAILABLE

NON-INVASIVE

QUANTITATIVE

WHOLE BRAIN

VERSATILE



VERSATILITY AND MULTI-SCALE

MULTIPLE TISSUE
PROPERTIES

STRUCTURE AND FUNCTION
CONNECTIVITY

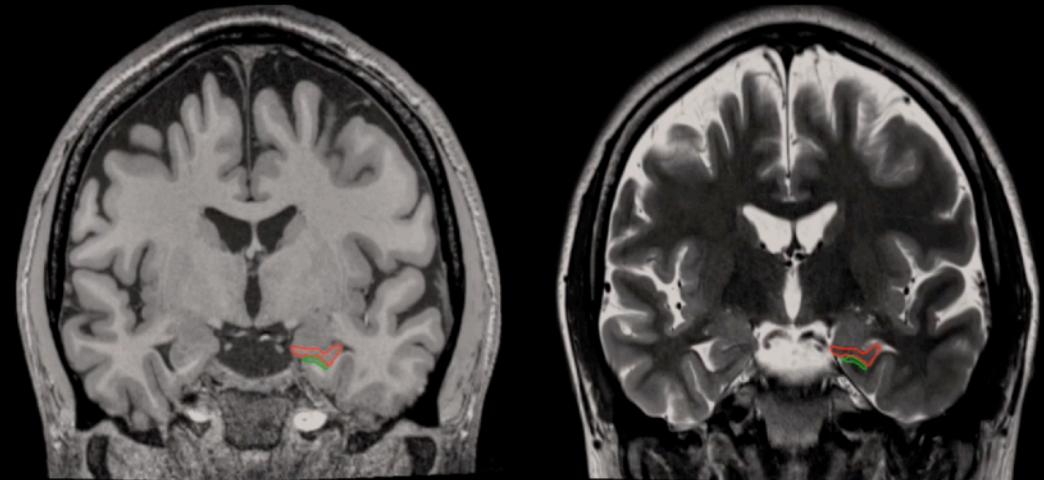
ROI AND WHOLE BRAIN
ANALYSIS

CONNECTIVITY

MACROSCALE NETWORK
MODELS



Courtesy of Alfred Anwander



Courtesy of Jessie Kulaga-Yoskovitz

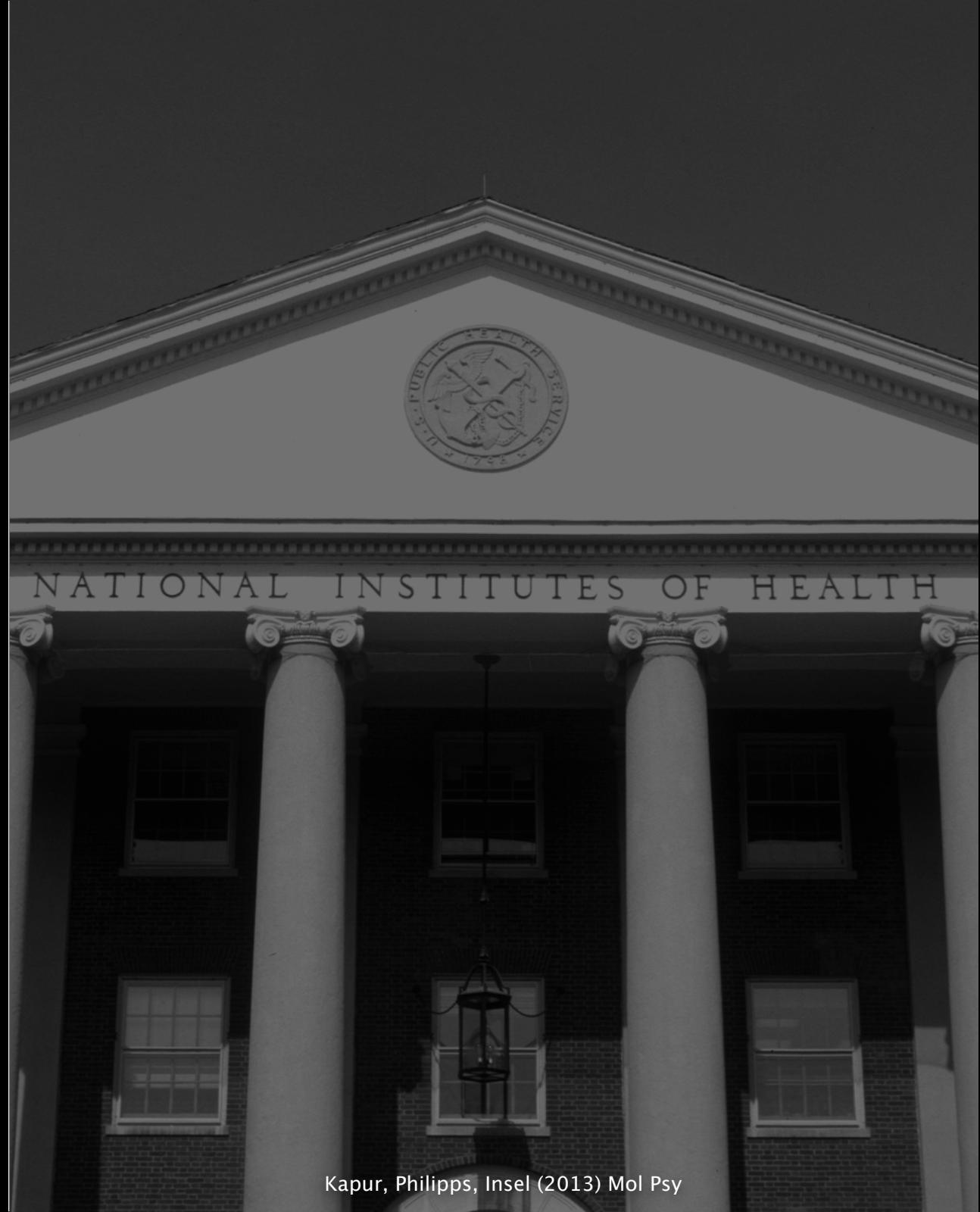
BRAIN PHENOTYPING IN HEALTH AND DISEASE

STRUCTURE, FUNCTION
& BEHAVIOR

BRAIN ORGANIZATION
AT MULTIPLE SCALES

MULTI-DIMENSIONAL PATIENT
PROFILING

CHALLENGE ESTABLISHED
CATEGORIES



Kapur, Philipps, Insel (2013) Mol Psy

OUTLINE

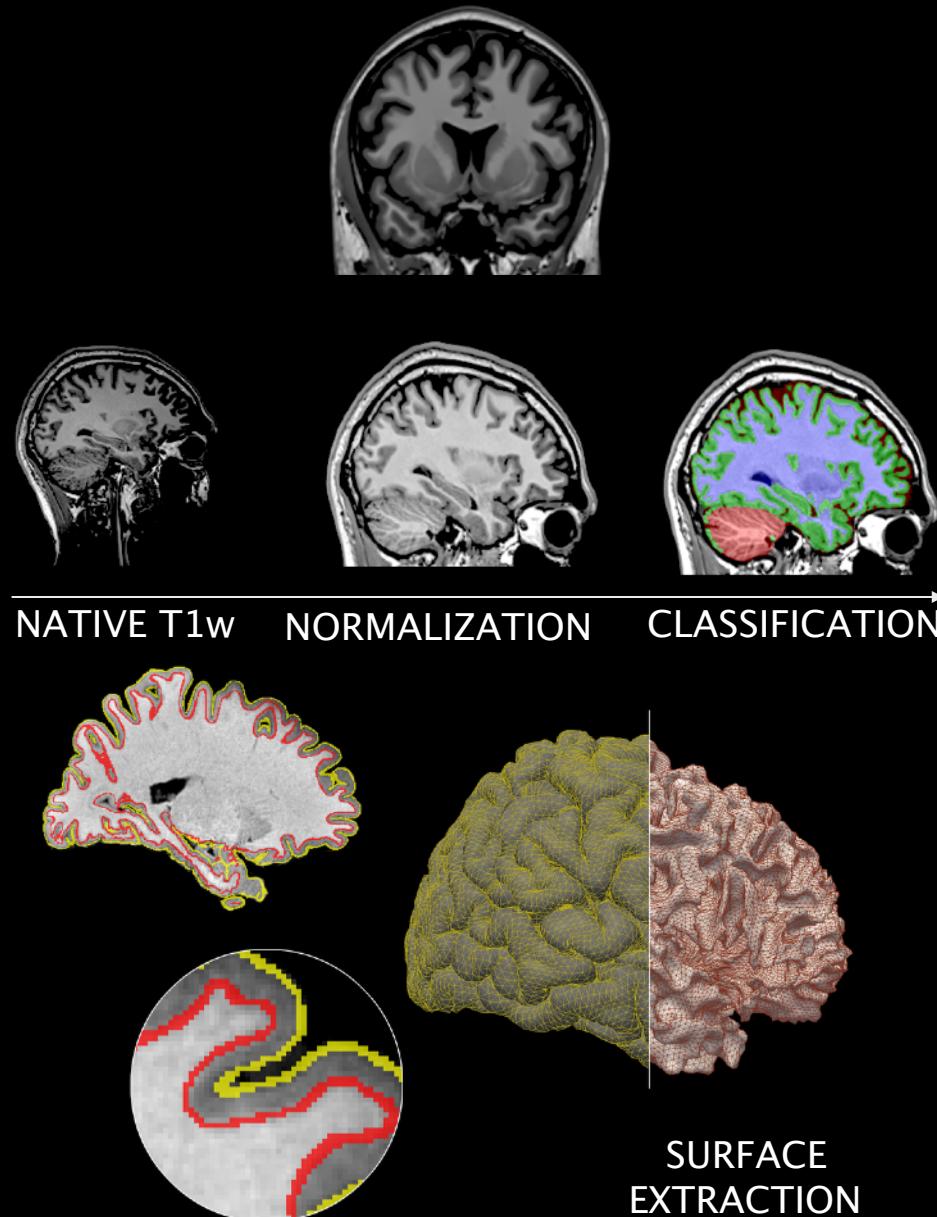
MULTIMODAL AND MULTISCALE MRI:
FROM CORTICAL MICROSTRUCTURE TO LARGE-SCALE NETWORKS

THE INTERPLAY BETWEEN HIPPOCAMPAL
ANATOMY, MICROSTRUCTURE, AND CONNECTOMICS

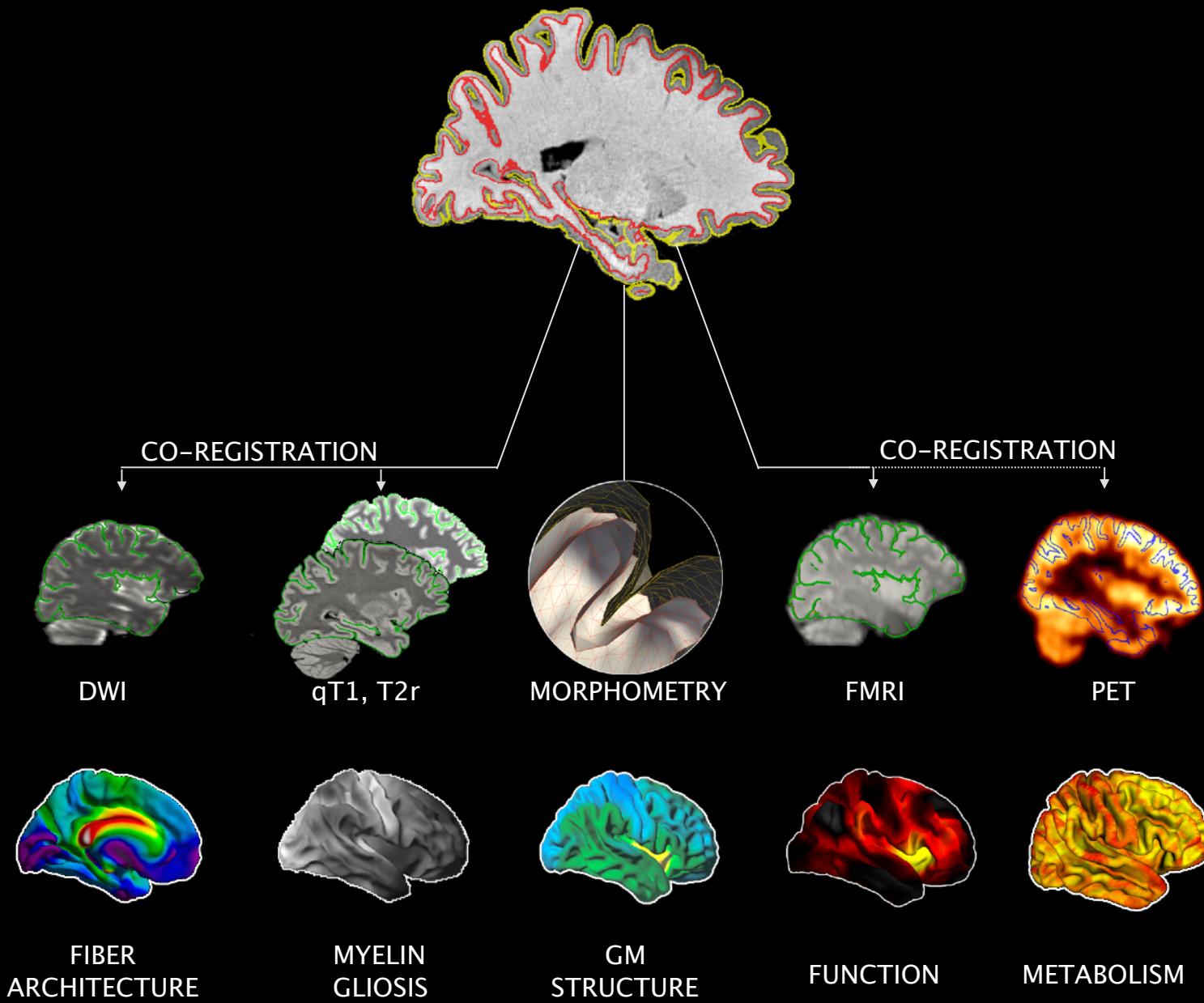
INTEGRATING HIGH-DEFINITION MRI WITH MACROSCALE NETWORK
MODELS IN TEMPORAL LOBE EPILEPSY

STUDY OF NEURODEVELOPMENT AND
DEVELOPMENTAL DISORDERS

MODELLING LOCAL STRUCTURE

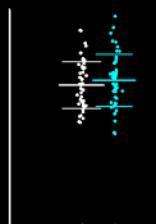
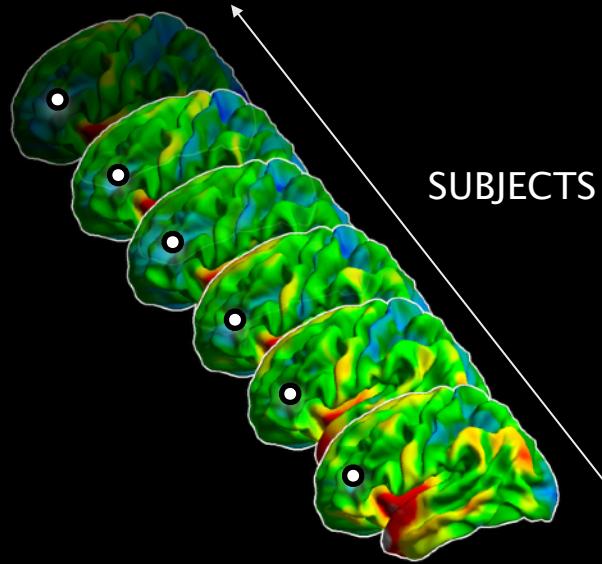


INTEGRATION OF MULTIPLE LOCAL MARKERS

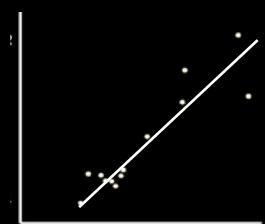


LOCO-REGIONAL STATISTICS

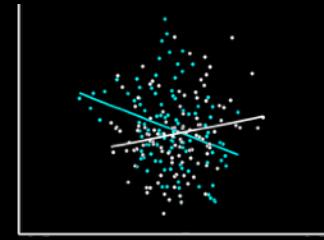
CROSS-SECTIONAL ANALYSES



$$Y = 1 + G$$

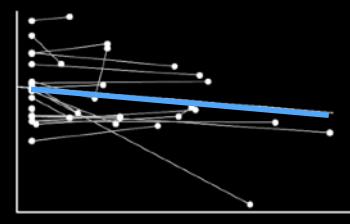
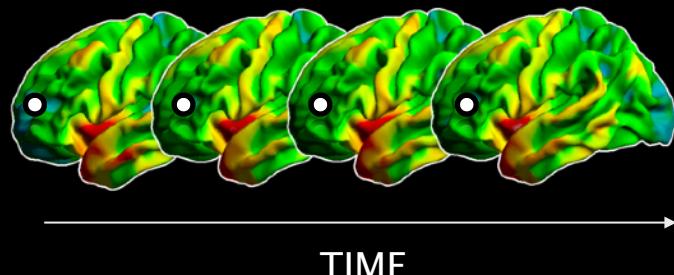


$$Y = 1 + A$$

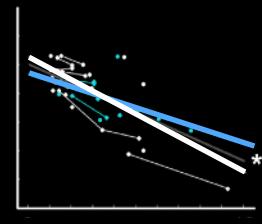


$$Y = 1 + G + A + G \times A$$

LONGITUDINAL ASSESSMENTS



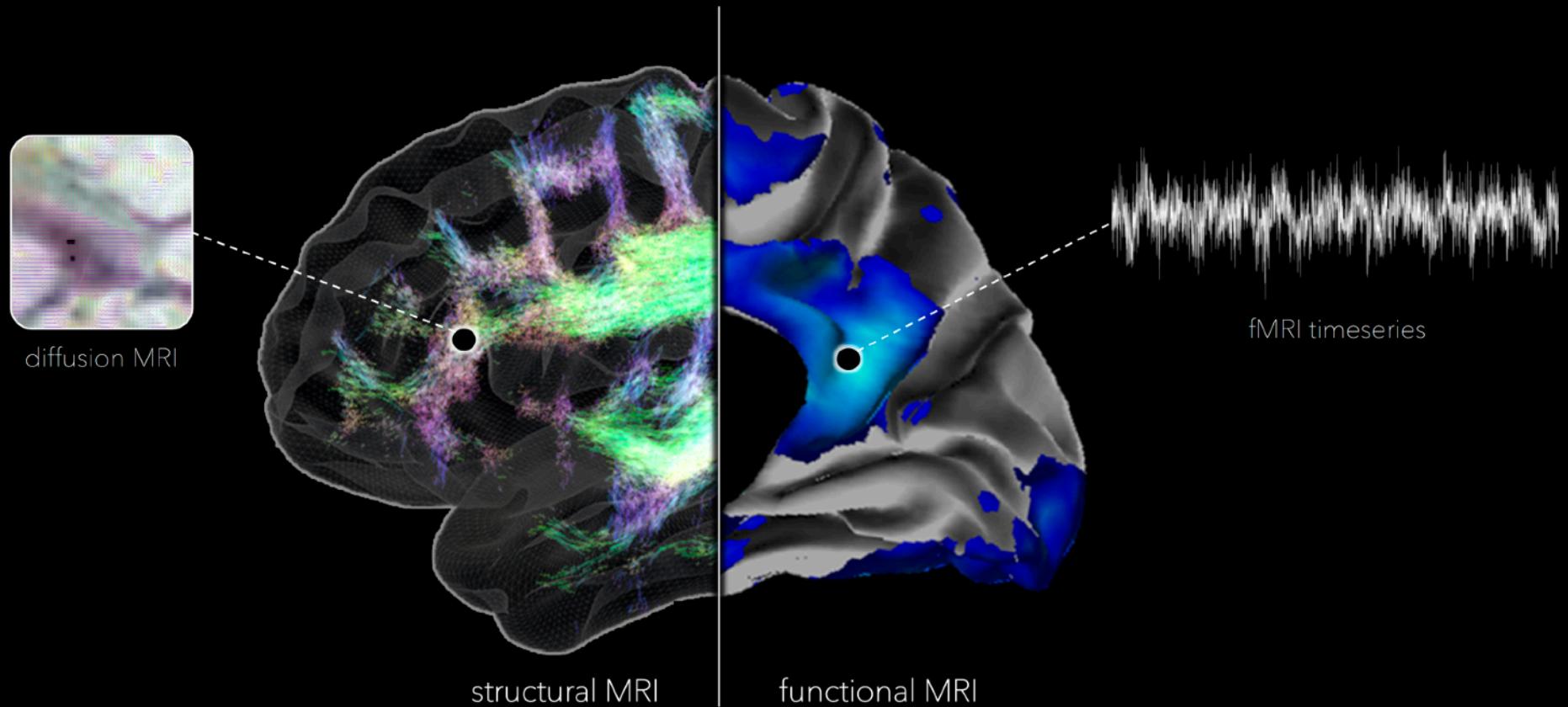
$$Y = 1 + r(S) + ISI$$



$$Y = 1 + r(S) + ISI + G + ISI \times G$$

Y is univariate or multivariate data

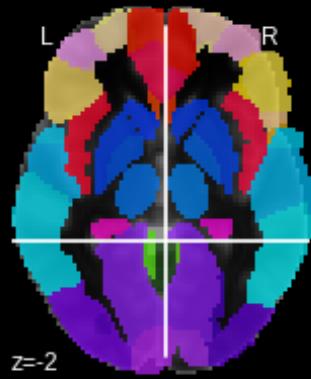
INTER-REGIONAL CONNECTIVITY



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

Biswal (1995) MRM
Friston (1994) HBM
Smith (2012) NIMG

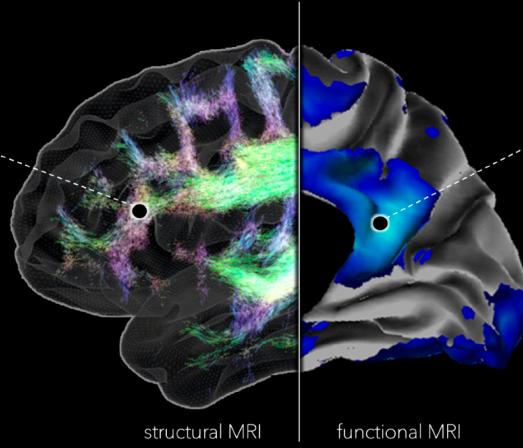
CONNECTOME ANALYSIS



Tzourio-Mazoyer (2002)
Neuroimage



diffusion MRI

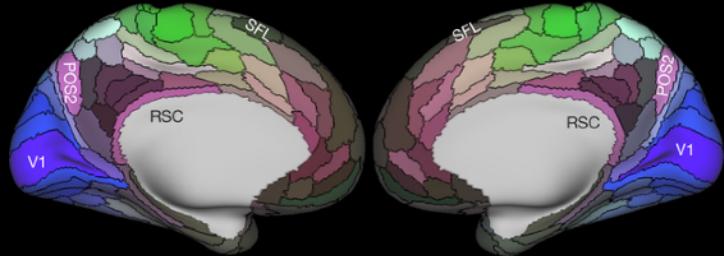
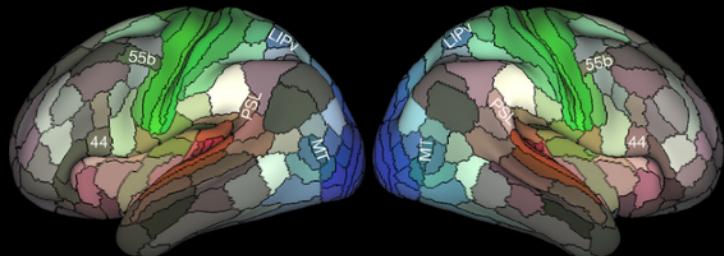


structural MRI

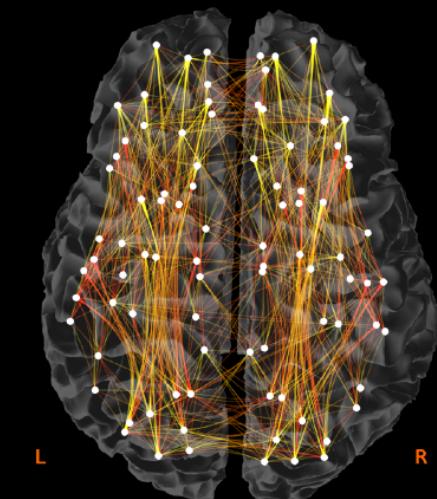
functional MRI



fMRI timeseries

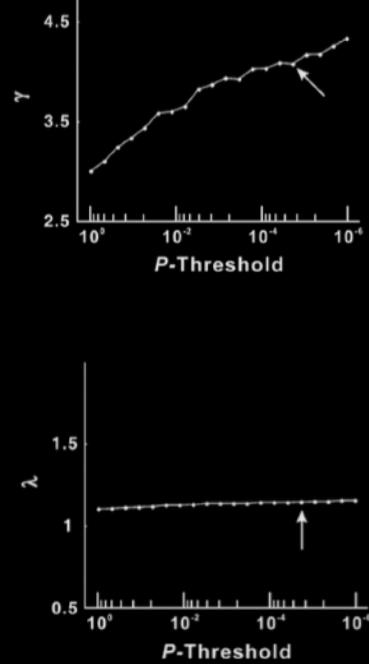
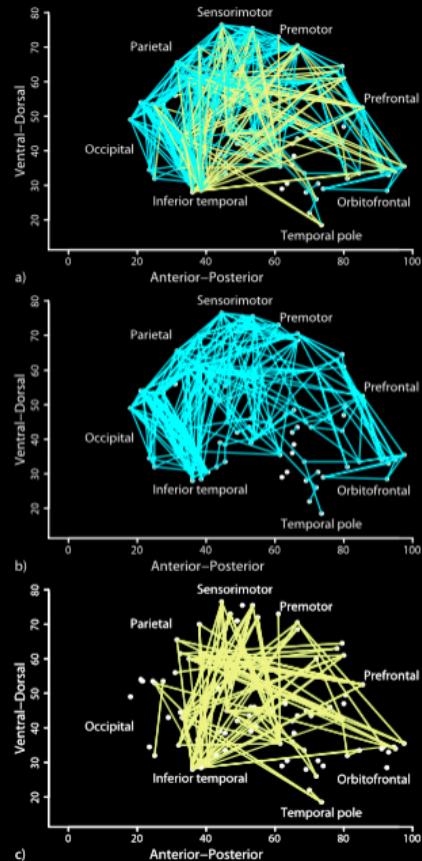


Glasser (2016) Nature



Bullmore and Sporns (2009) NRN

MACROSCALE: SMALL WORLD TOPOLOGY



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

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

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

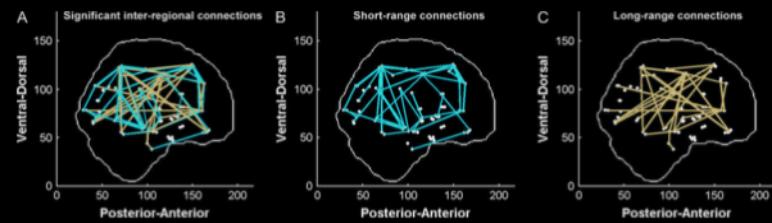
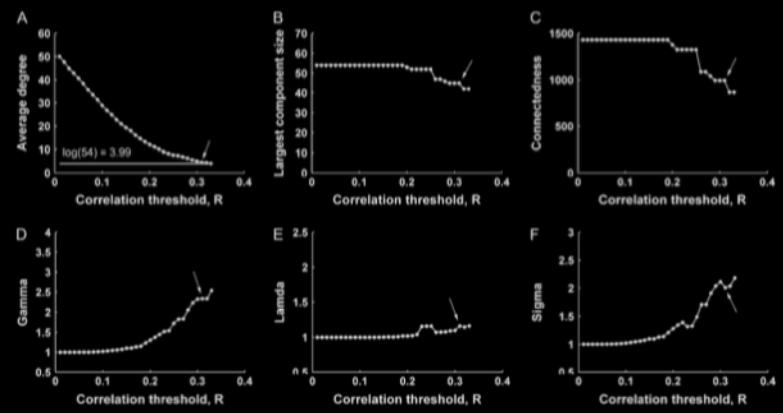
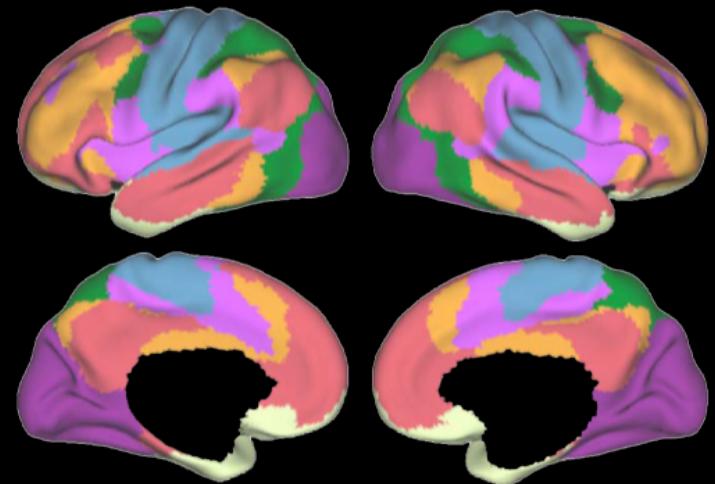
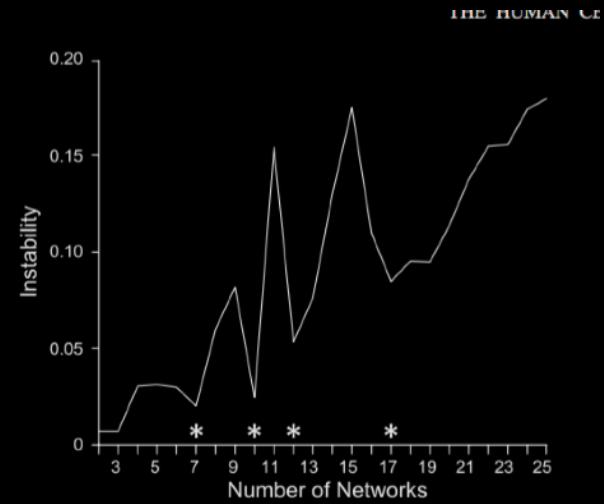
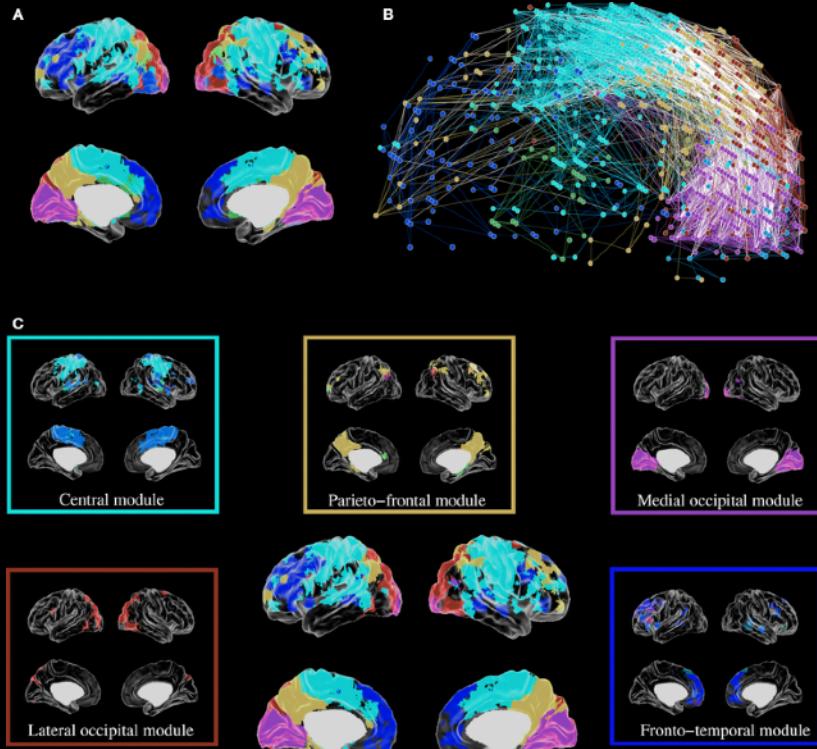


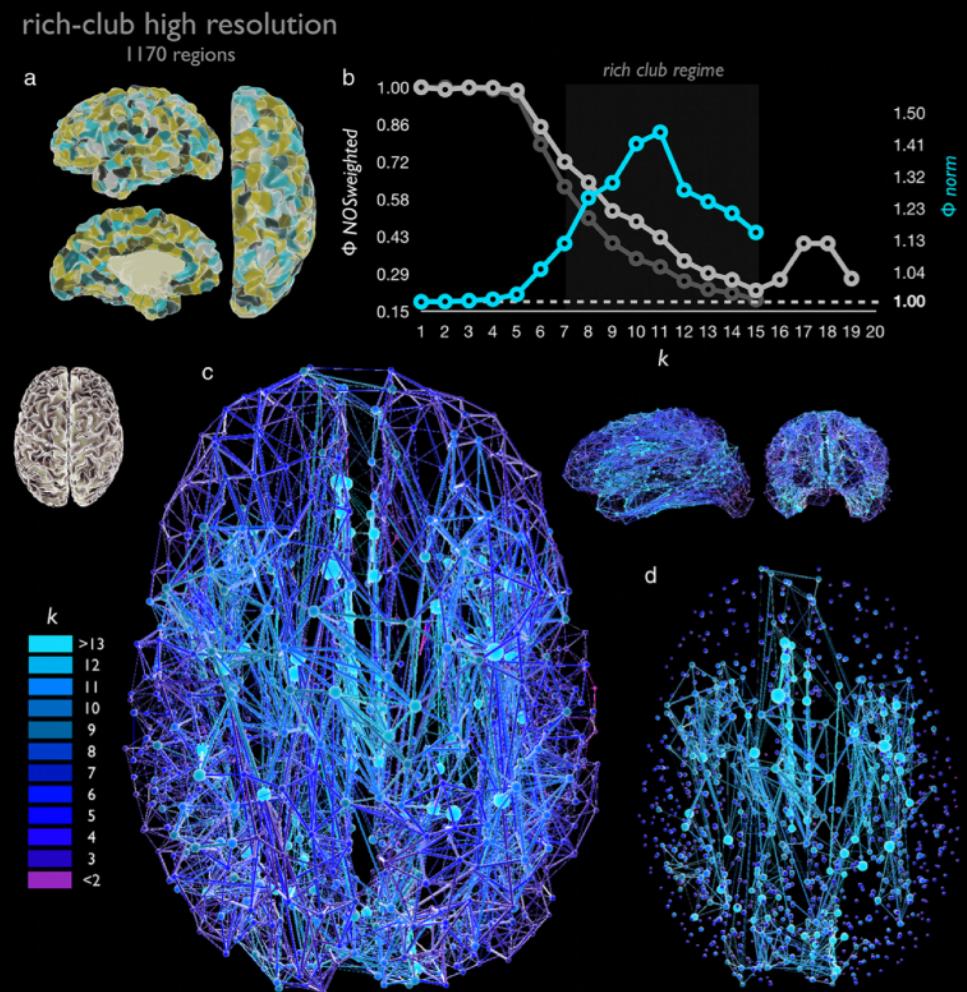
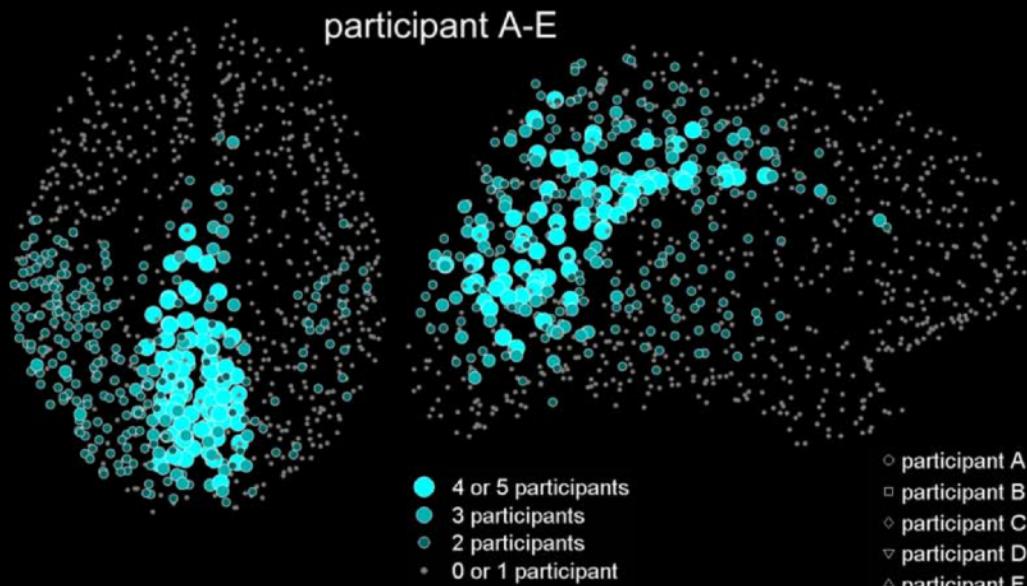
Figure 3. Short- and long-range anatomical connections in the anatomical space. (A) One hundred and four undirected edges ($1 - 7.3\%$ of the 1431 possible connections among regions) representing the significant connections were shown in a sagittal view of the brain. Edges were classified into (B) short-range 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.



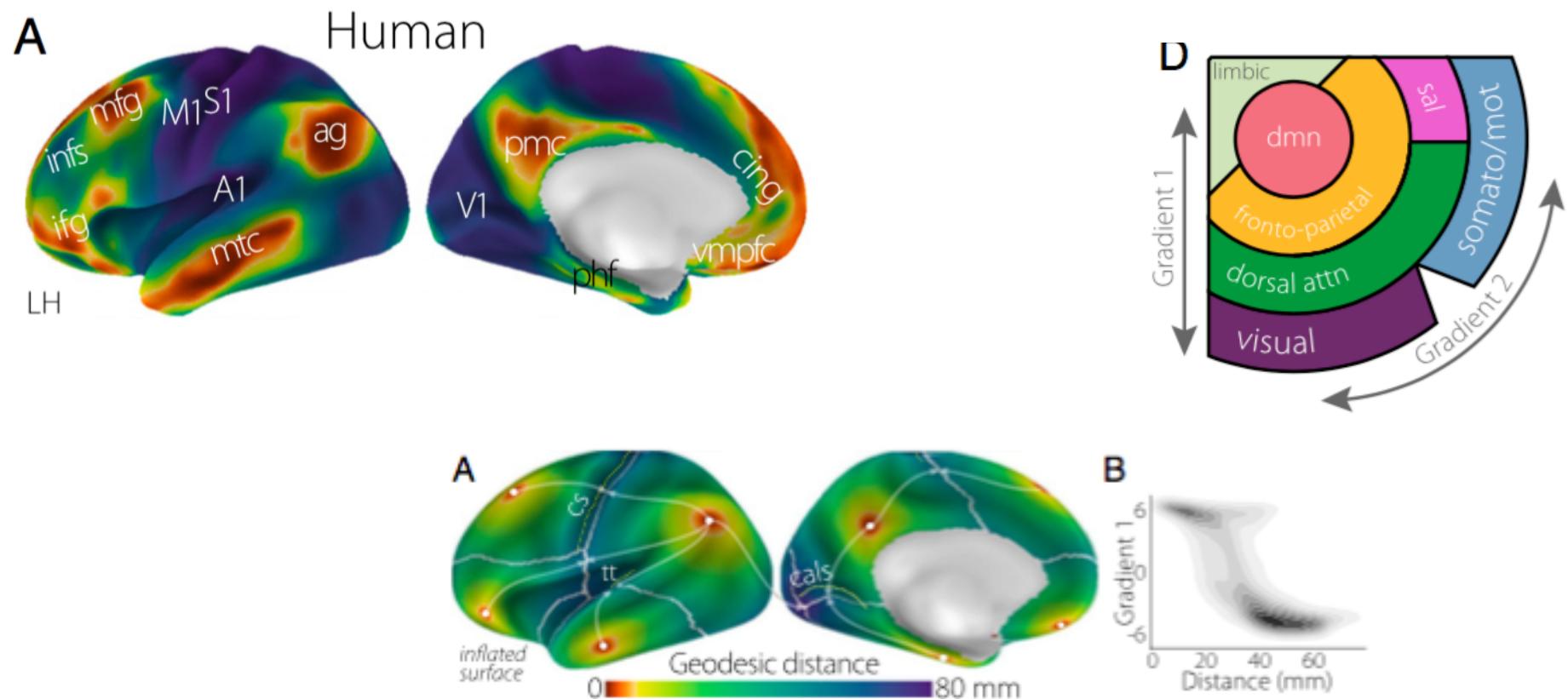
MACROSCALE: MODULARITY

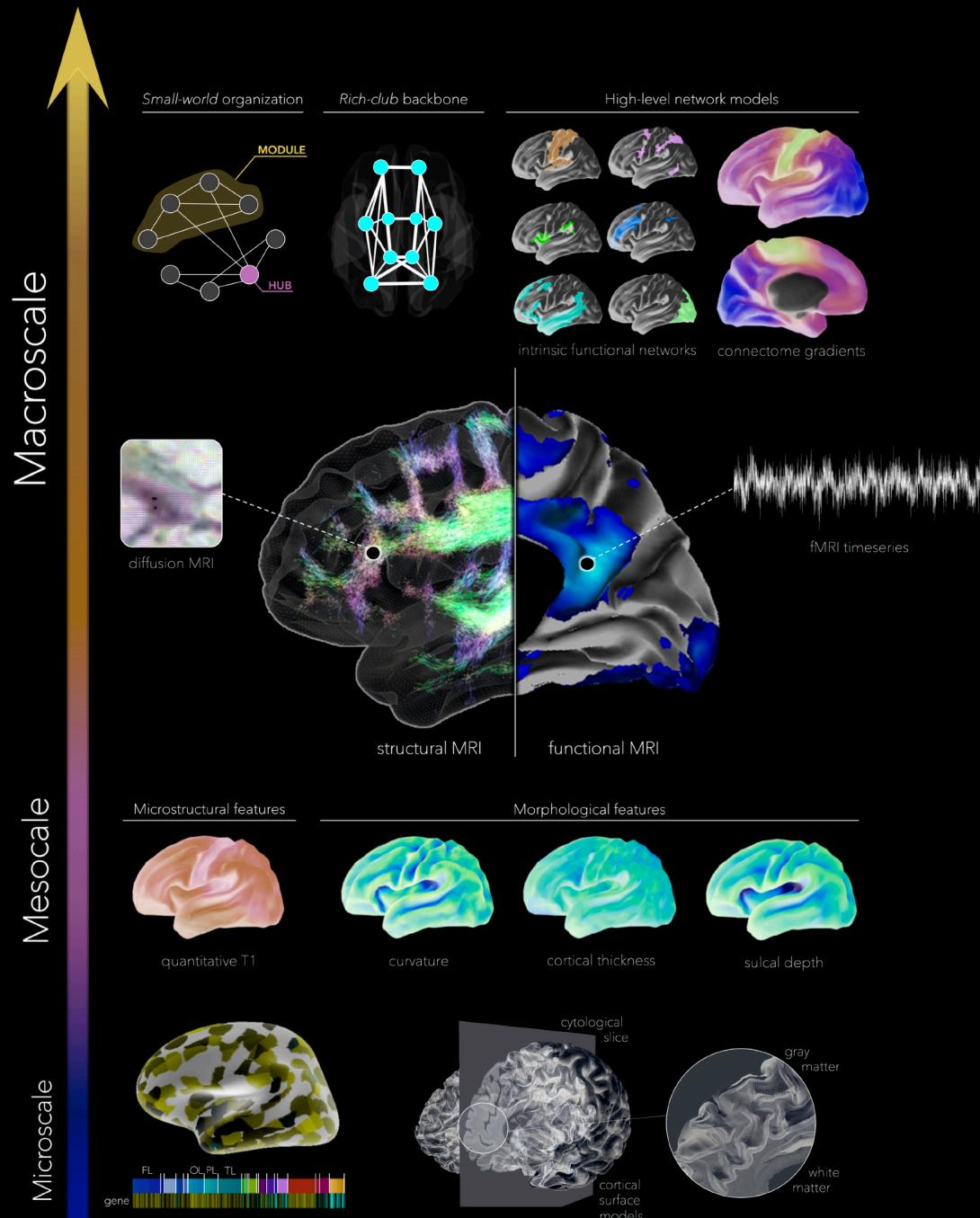


MACROSCALE: CORE-PERIPHERY



MACROSCALE: CONNECTOME COMPRESSION & GRADIENTS







MULTI-SCALE STUDIES OF THE
MESIOTEMPORAL LOBE
AND TEMPORAL LOBE EPILEPSY

METHODOLOGY
&
ANALYTICS

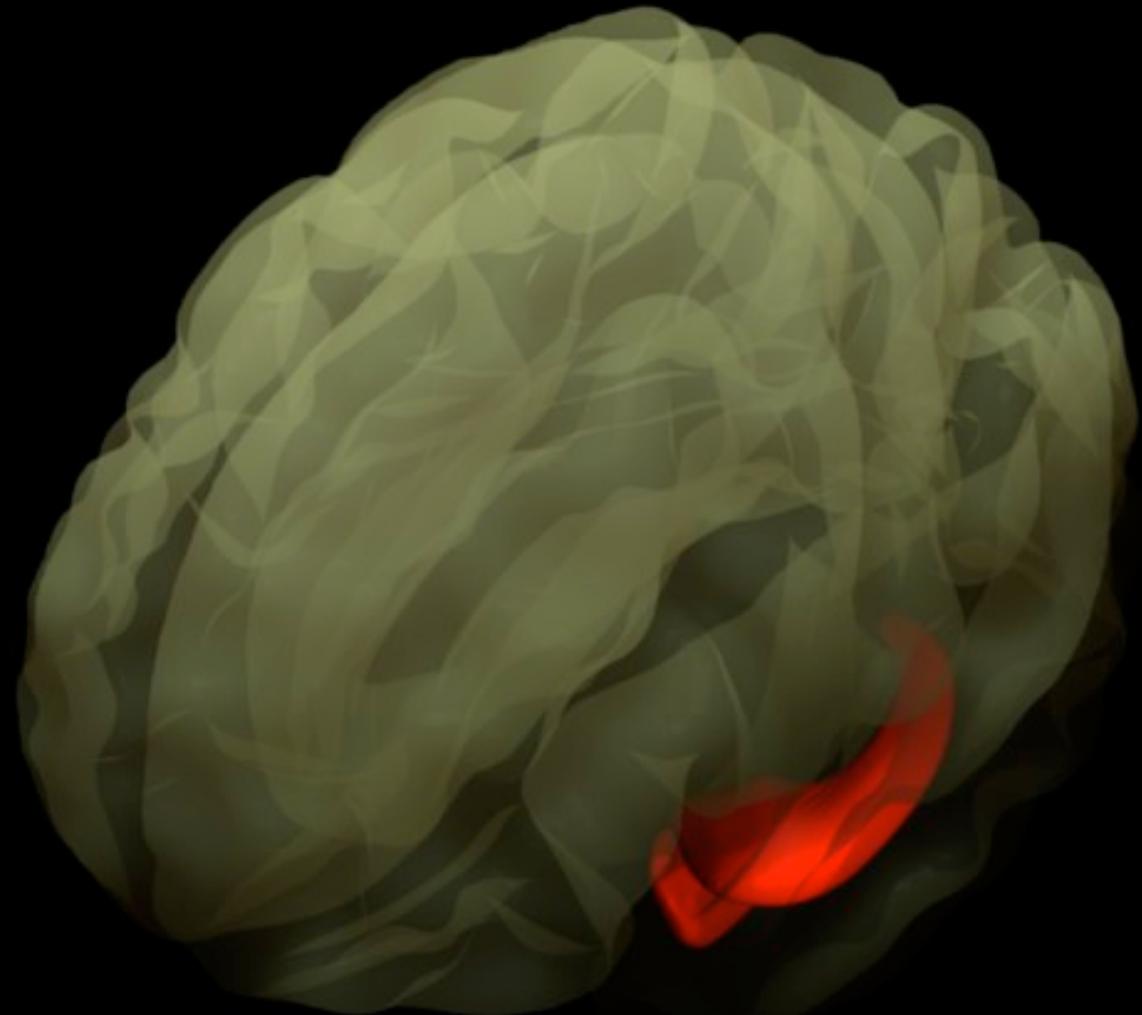
STRUCTURE-FUNCTION
ANALYSIS OF TYPICAL AND ATYPICAL
BRAIN DEVELOPMENT

THE HIPPOCAMPUS

KEY ROLE IN NUMEROUS
COGNITIVE PROCESSES

ASSOCIATED TO SEVERAL
IMPORTANT BRAIN NETWORKS

AFFECTED ACROSS
MULTIPLE BRAIN DISORDERS



THE HIPPOCAMPUS

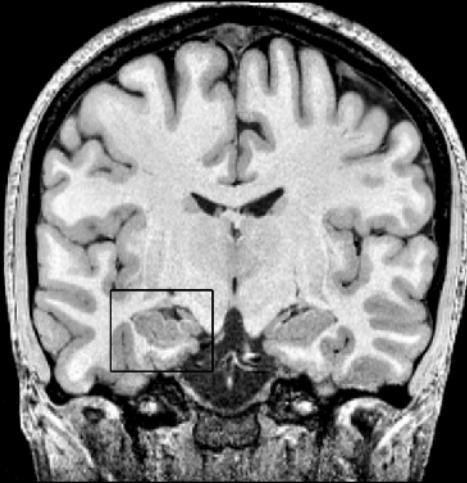
OFTEN TREATED AS
SINGLE STRUCTURE

HOWEVER:
COMPLEX STRUCTURE

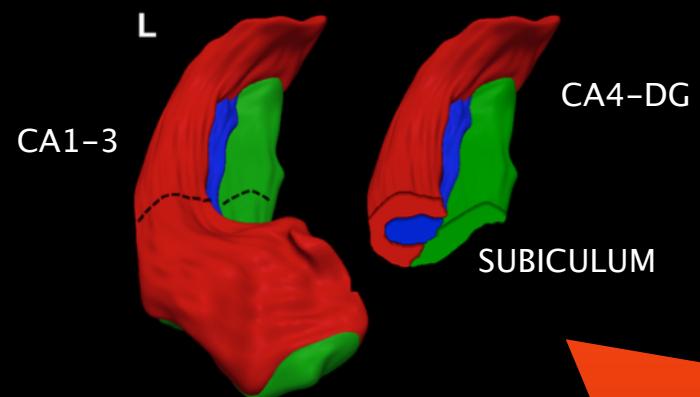
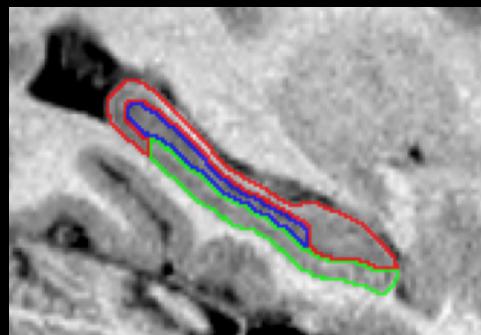
COMPOSED OF SEVERAL SUBFIELDS

LONG-AXIS SPECIALIZATION

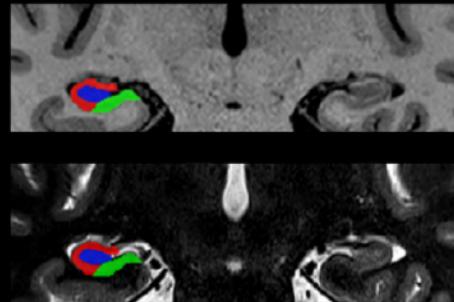




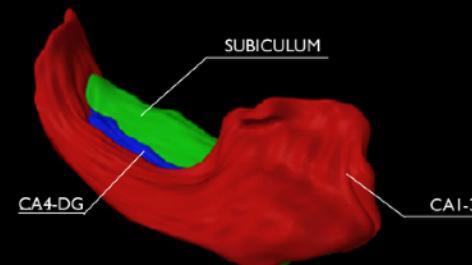
<https://www.nitrc.org/projects/mni-hisub25/>



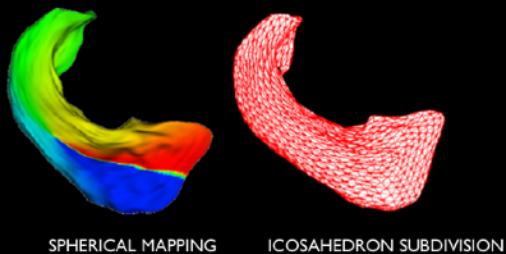
A SUBFIELD LABEL



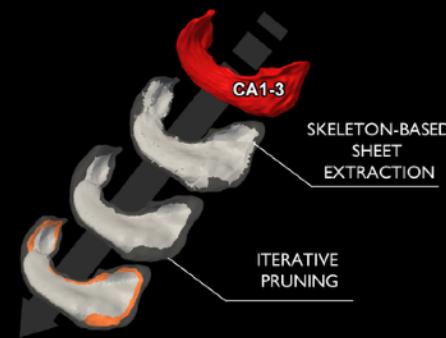
B SUBFIELD HULL REPRESENTATION



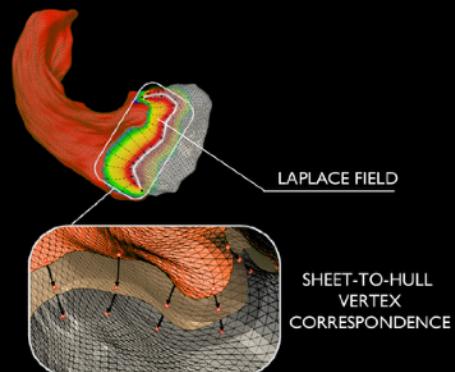
C SPHARDM-PDM PARAMETRIZATION OF OUTER HULL



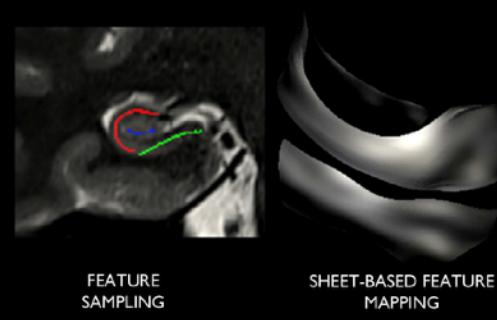
D GENERATION OF MEDIAL SHEET

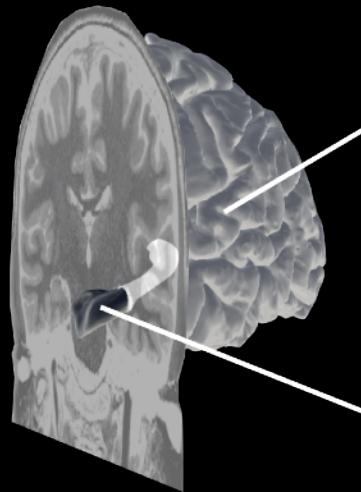
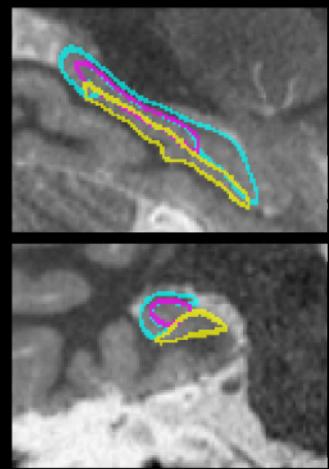


E PROPAGATING PARAMETRIZATION TO SHEET



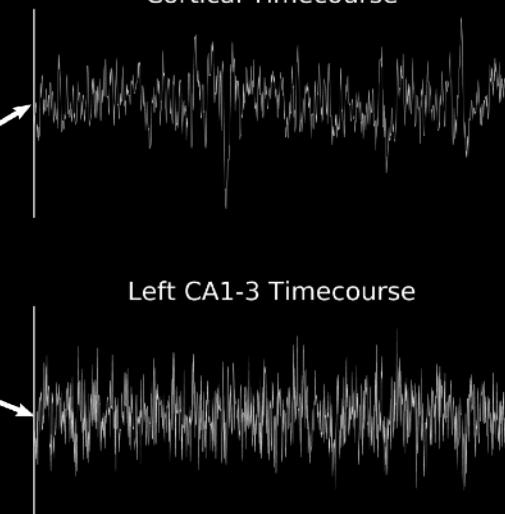
F SHEET-BASED MEASURES



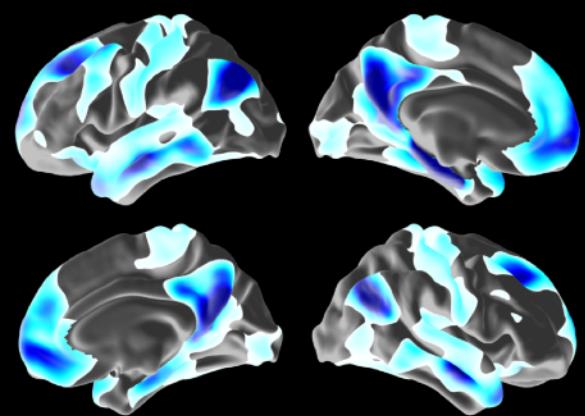


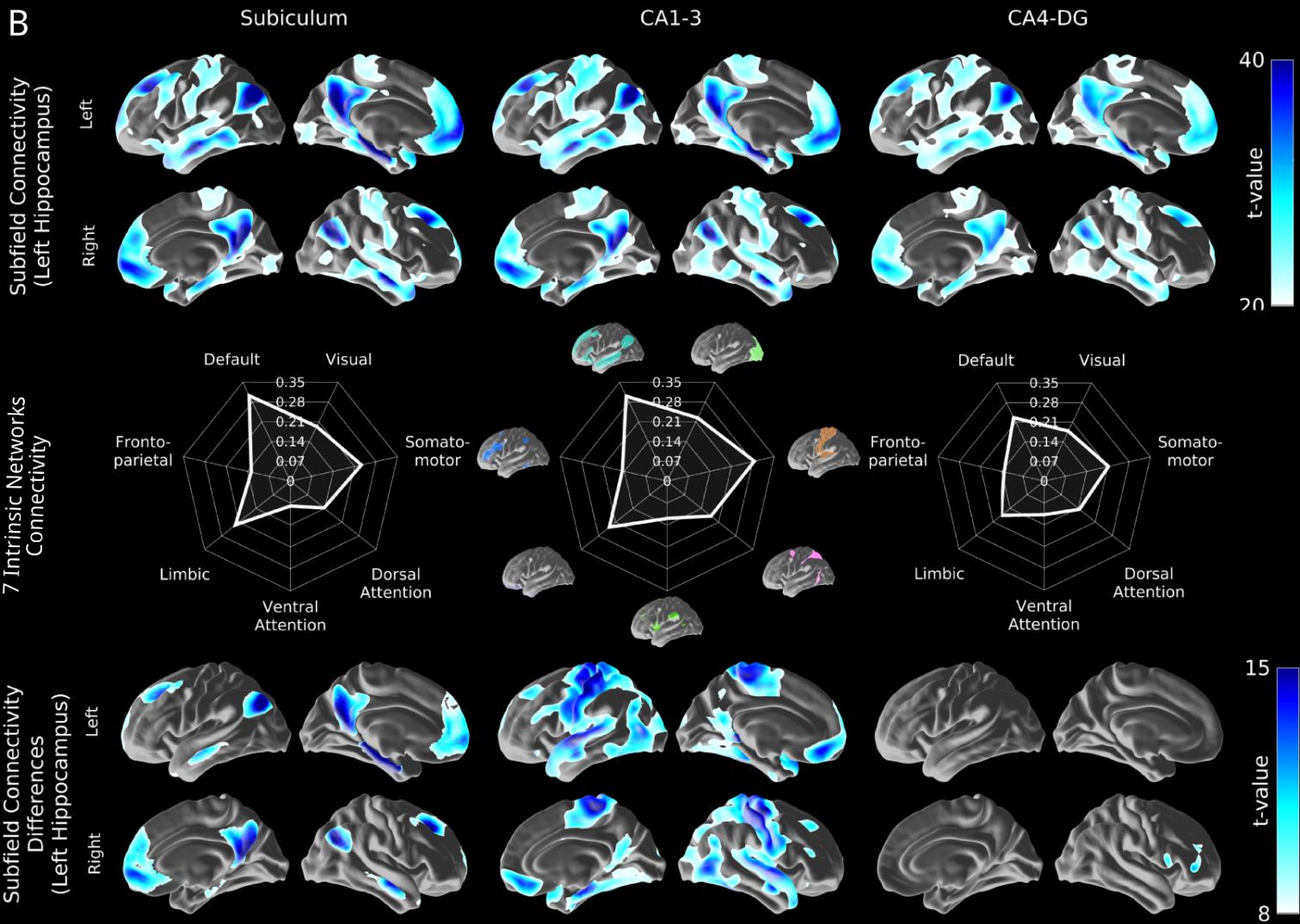
Cortical Timecourse

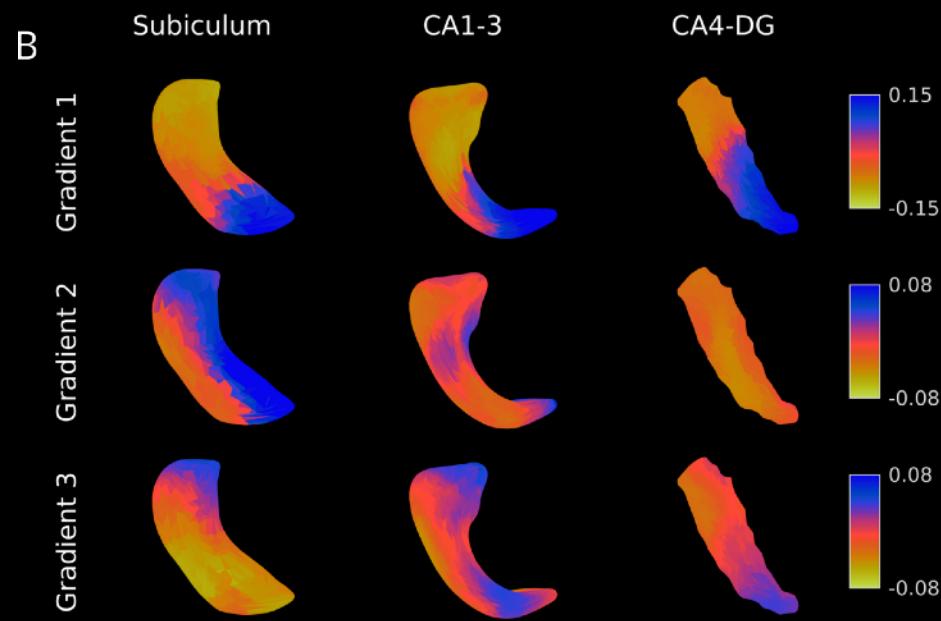
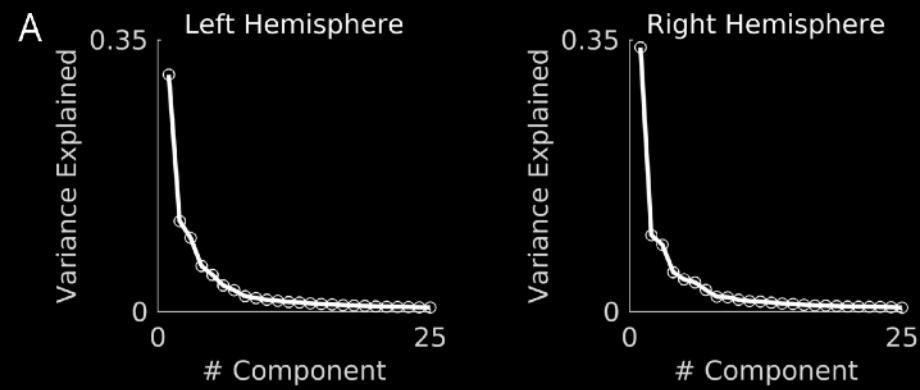
Left CA1-3 Timecourse

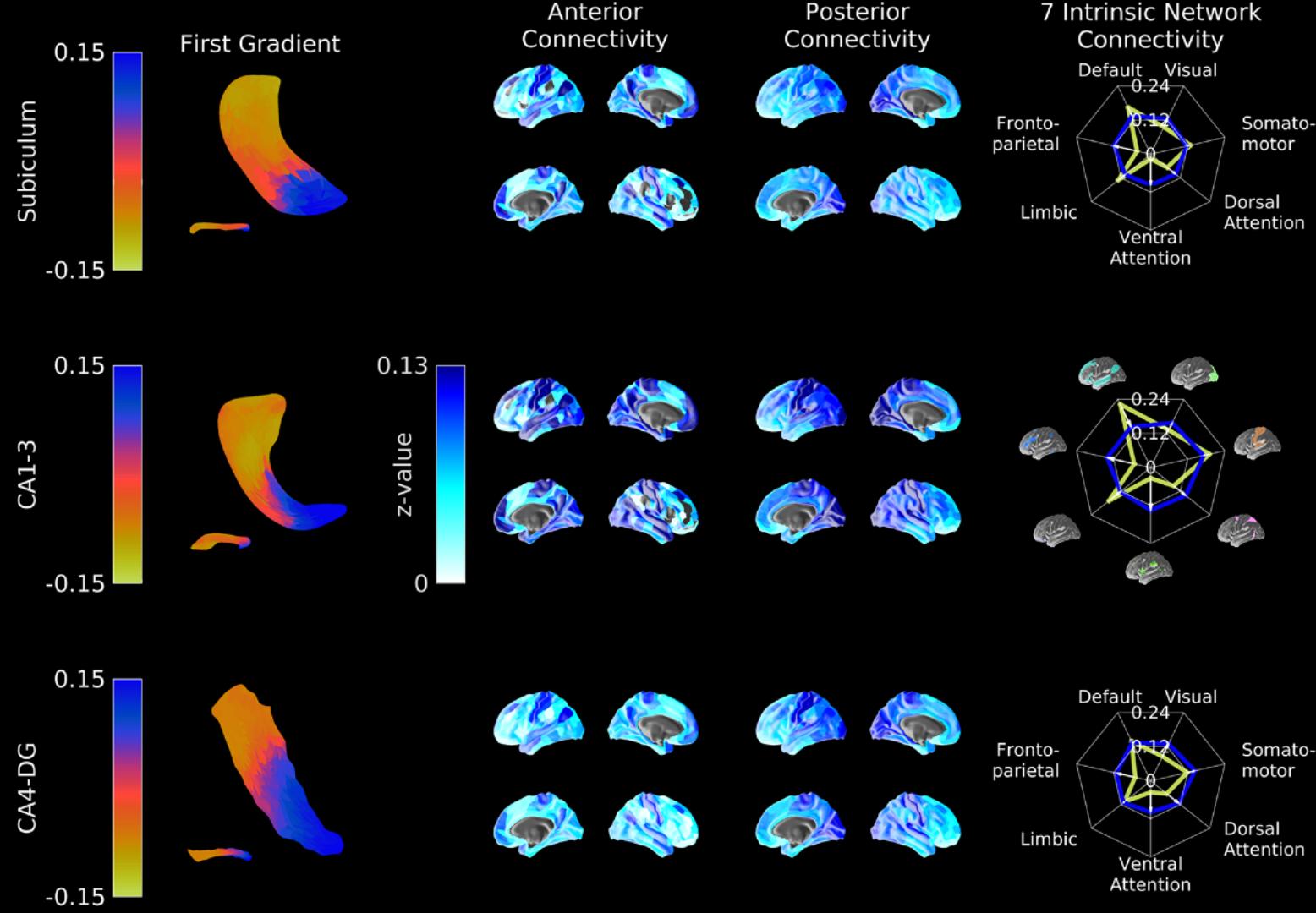


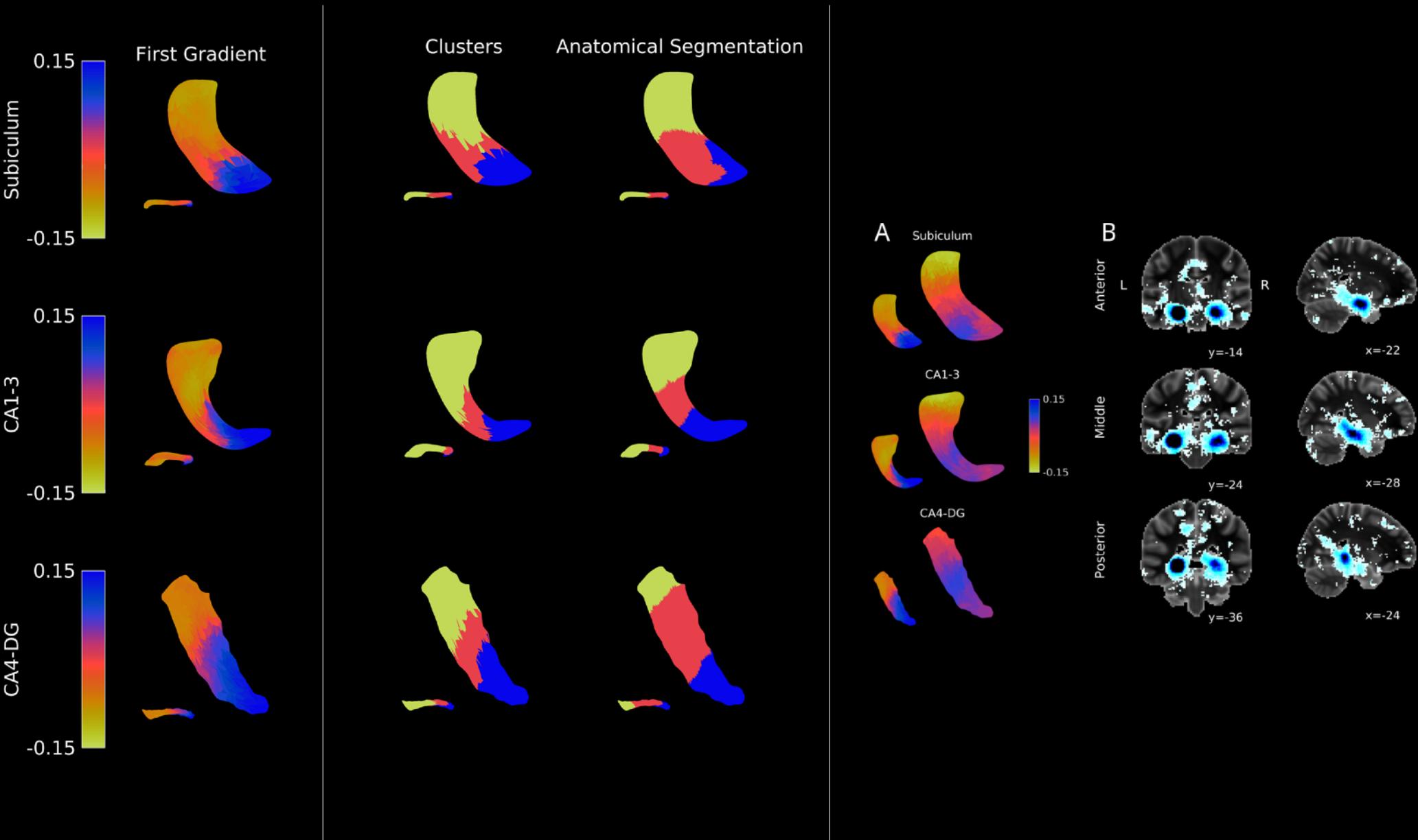
Subfield-Cortical Connectivity



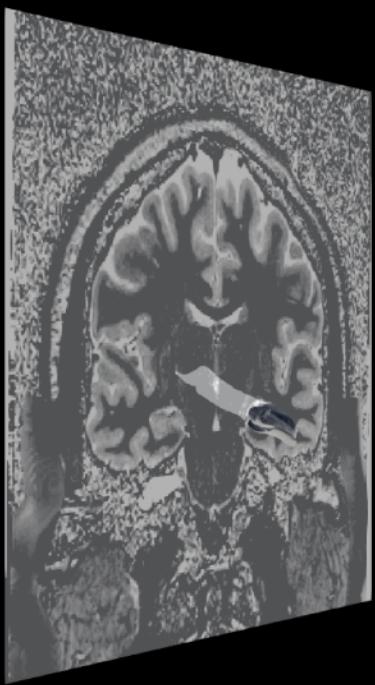
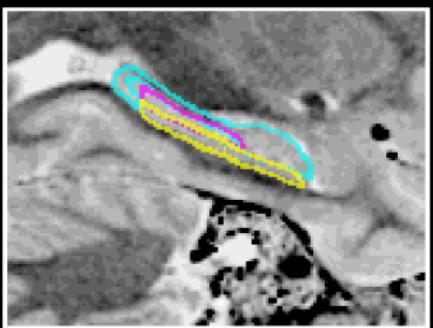
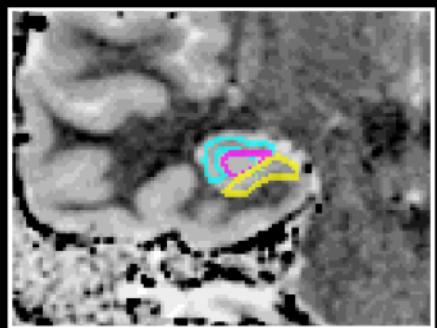






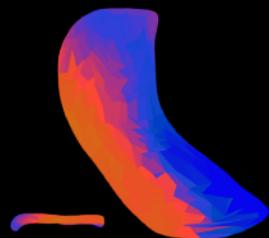


A



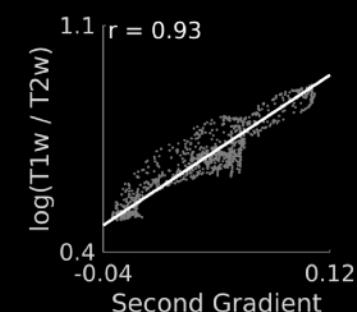
B

Second Gradient

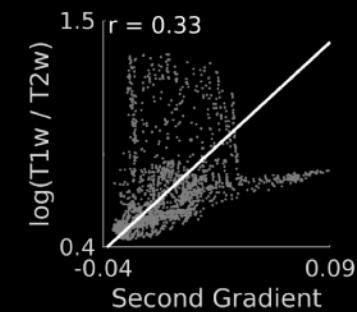
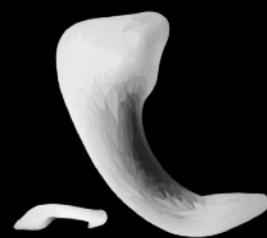
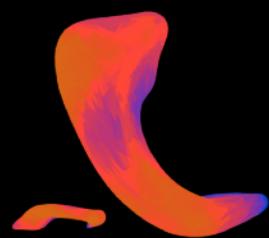


Subiculum

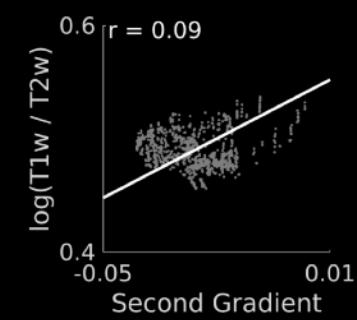
T1w / T2w

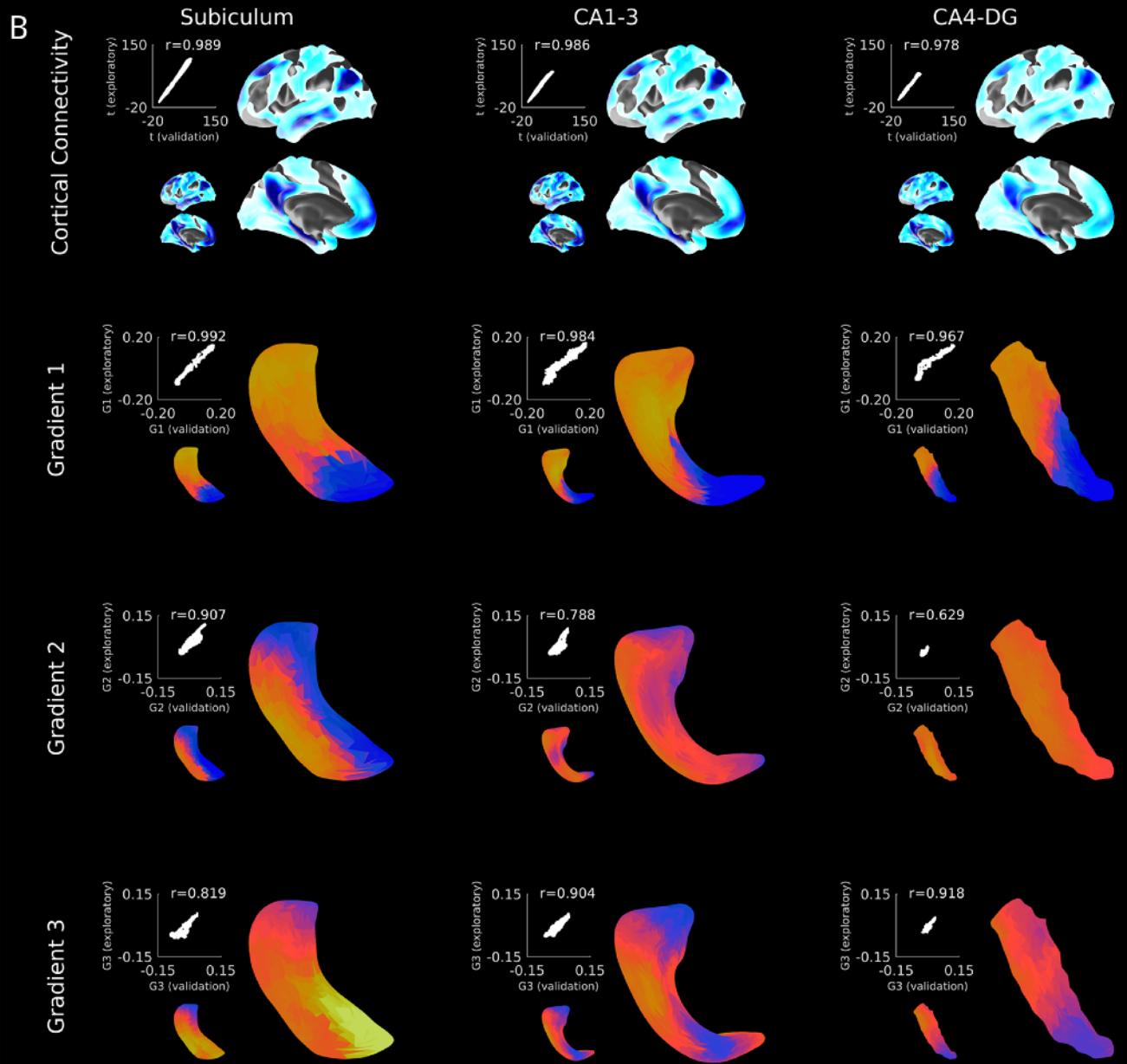
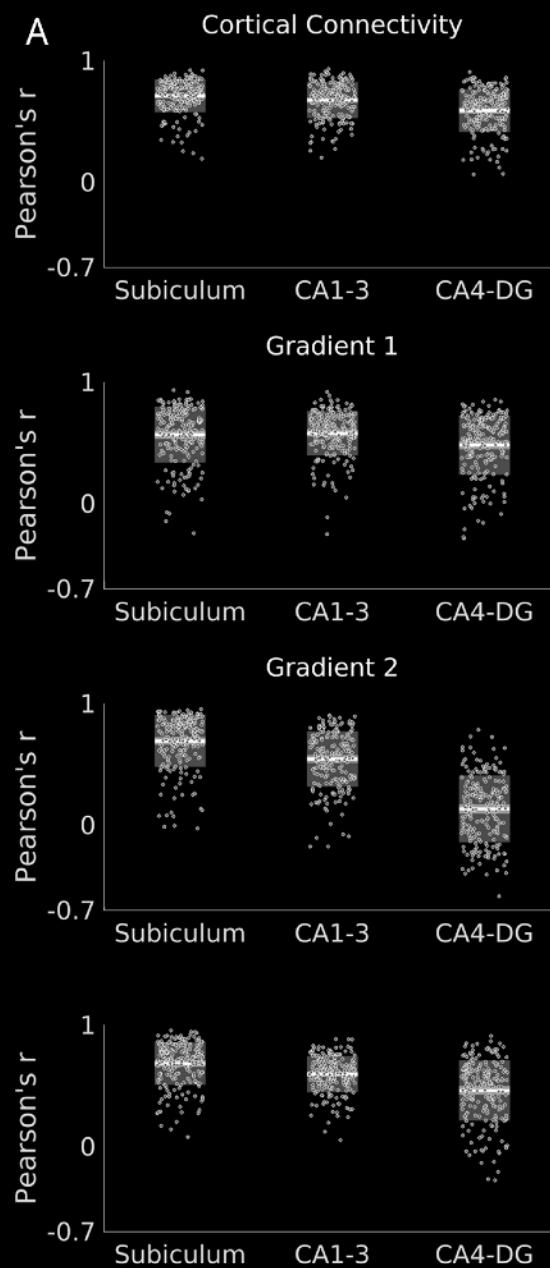


CA1-3



C4-DG





INTERIM SUMMARY: HIPPOCAMPUS

SURFACE-BASED ANALYTICS:
INTEGRATE SUBFIELD MARKERS OF
STRUCTURE AND CONNECTIVITY ALONG A-P EXTENT

MAP COMMON AND UNIQUE
SUBFIELD CONNECTIVITY “FINGERPRINTS”

GRADIENT BASED TECHNIQUES EVALUATE
WITHIN-SUBFIELD CHANGES IN CONNECTIVITY

G1: RELATION TO
LONG-AXIS SPECIALIZATION

G2: MEDIO-LATERAL GRADIENT
ASSOCIATED TO MICROSTRUCTURE

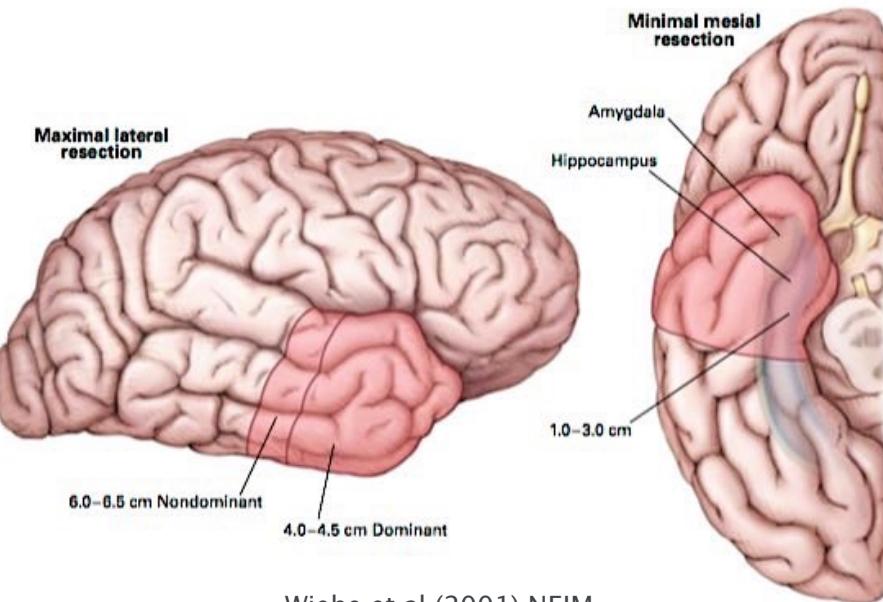
TEMPORAL LOBE EPILEPSY

ONE OF THE MOST COMMON
DRUG-RESISTANT
EPILEPSIES IN ADULTS

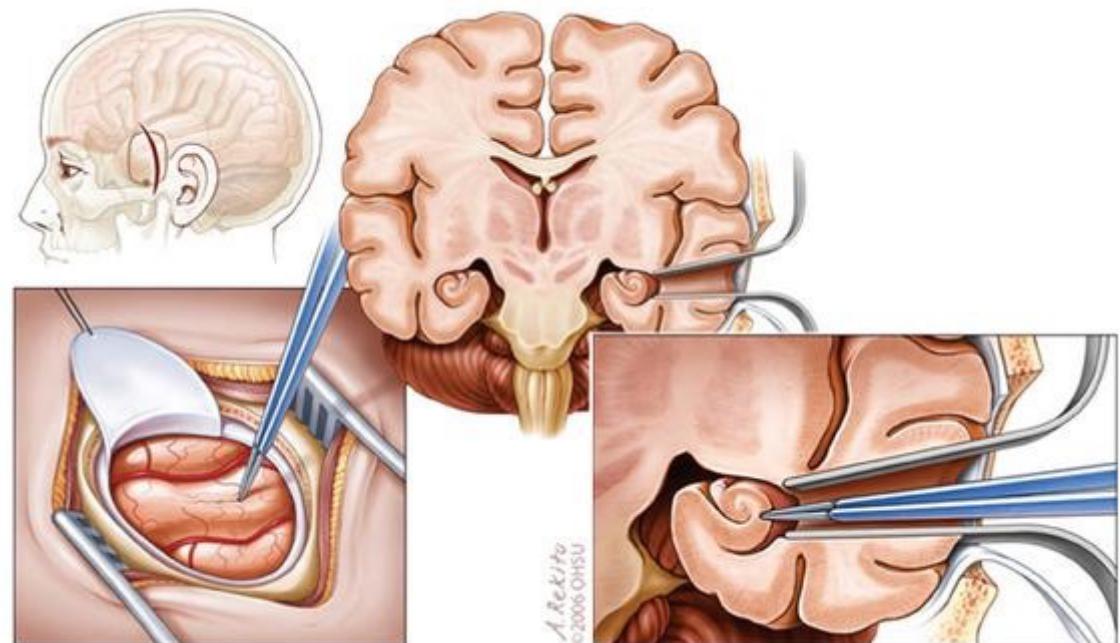
SEIZURES ARISING FROM TL

SURGERY MOST EFFECTIVE
TREATMENT

ASSOCIATED WITH
HIPPOCAMPAL SCLEROSIS (HS)



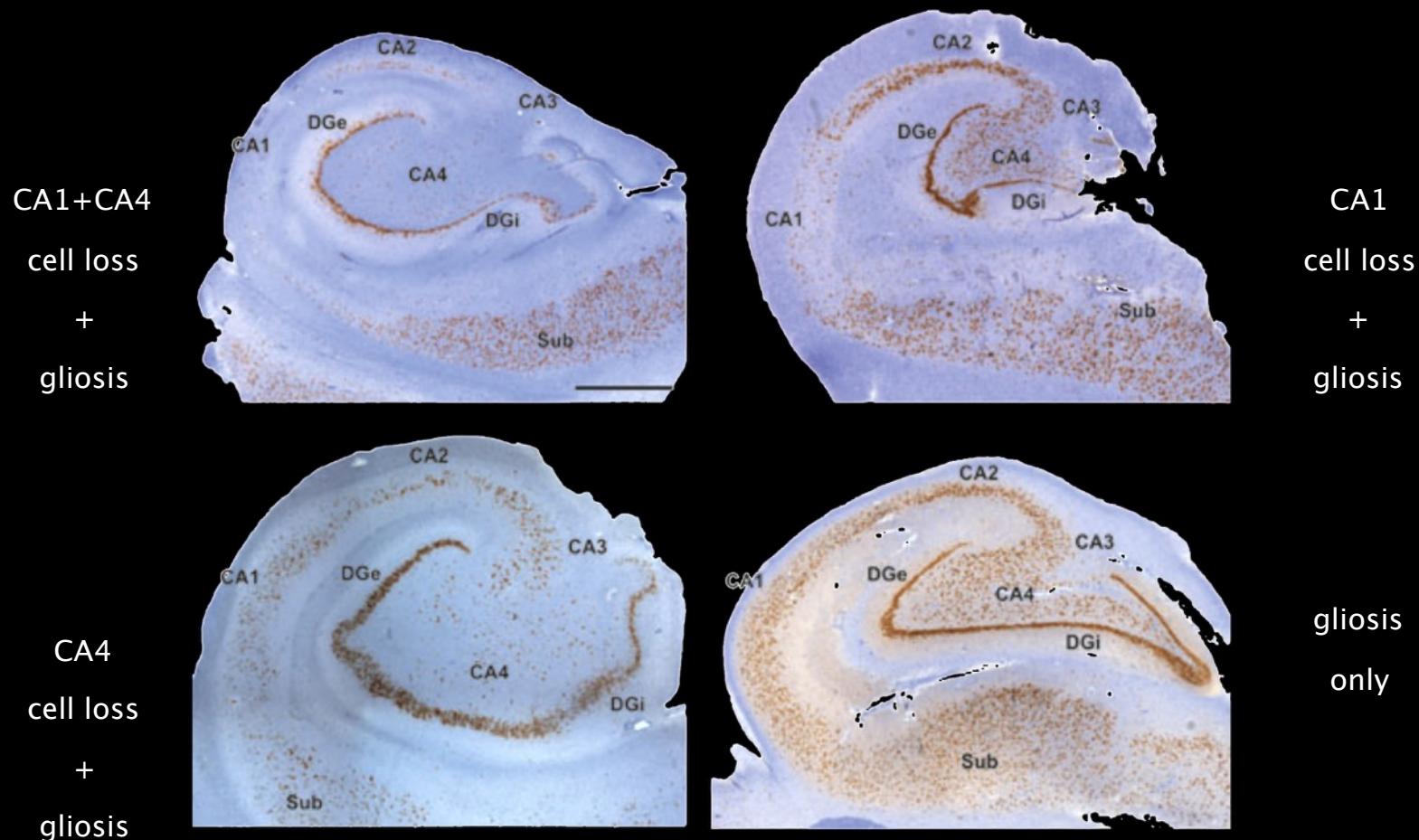
Wiebe et al (2001) NEJM



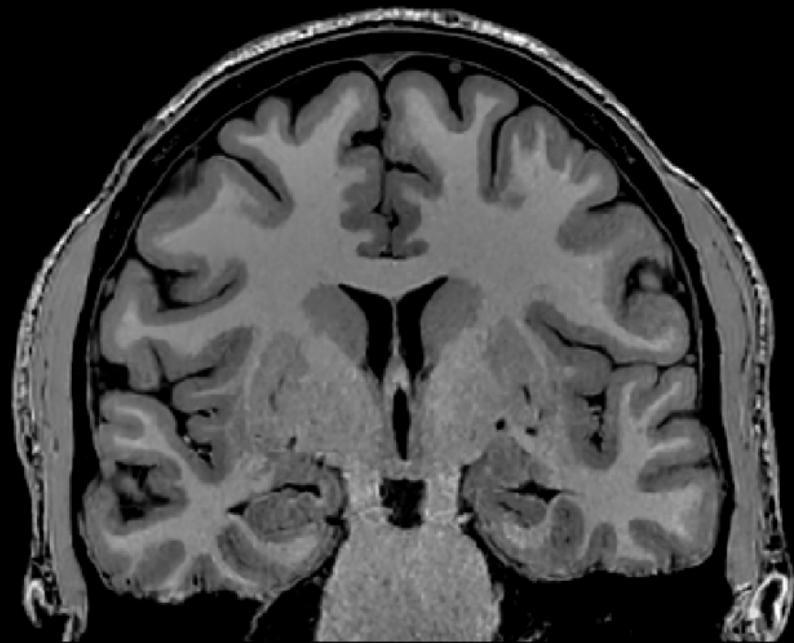
Spencer & Burchiel (2012) Epilepsy Research and Treatment

TEMPORAL LOBE EPILEPSY

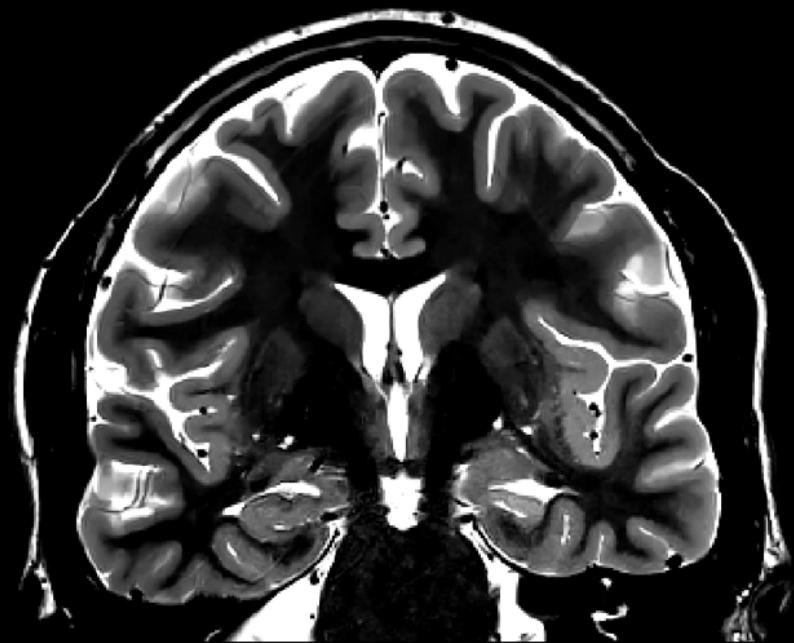
HS IS THE TLE HALLMARK BUT NOT A SINGLE ENTITY



THE CONTRIBUTIONS OF NEUROIMAGING TO TLE EVALUATION AND DIAGNOSIS OF HS



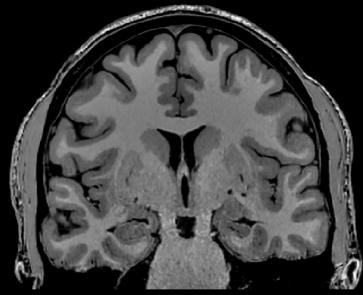
T1-weighted



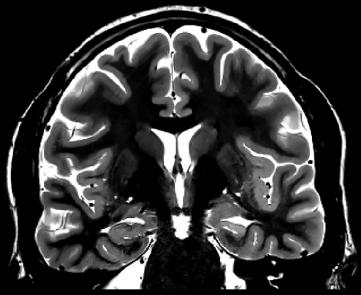
T2-weighted

STUDY DESIGN

24



T1-weighted



T2-weighted

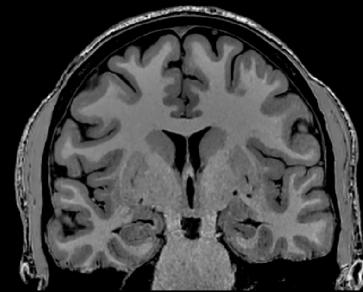


SURGERY

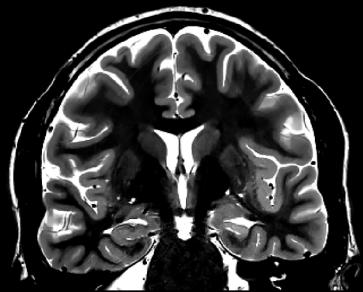


HS

19



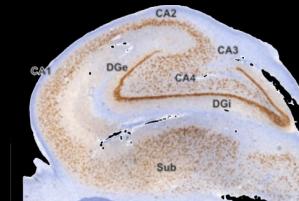
T1-weighted



T2-weighted

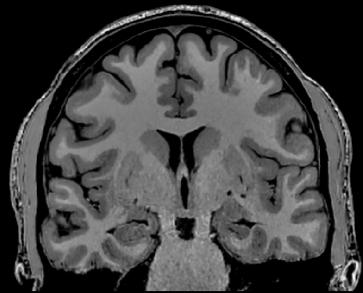


SURGERY

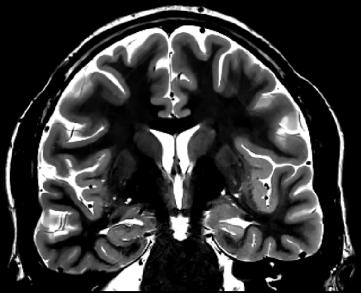


GLIOSIS

25



T1-weighted



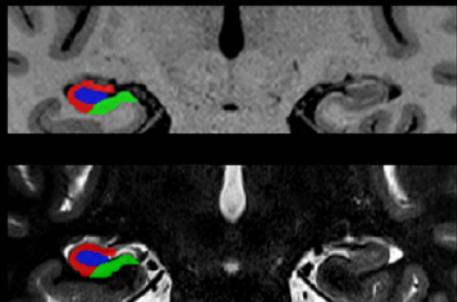
T2-weighted

3T MRI DATA

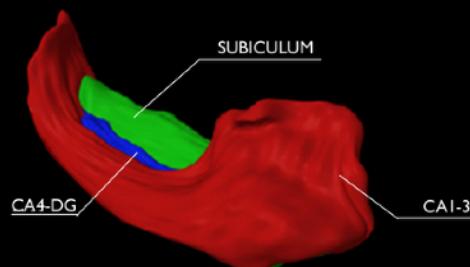
CONTROLS

IMAGE PROCESSING

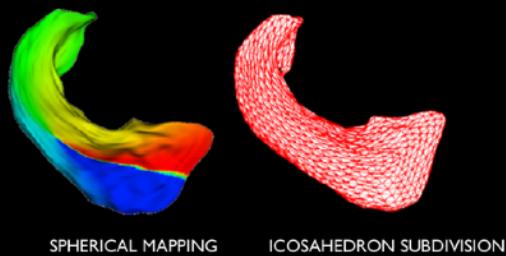
A SUBFIELD LABEL



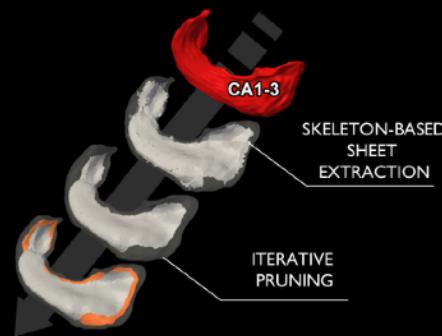
B SUBFIELD HULL REPRESENTATION



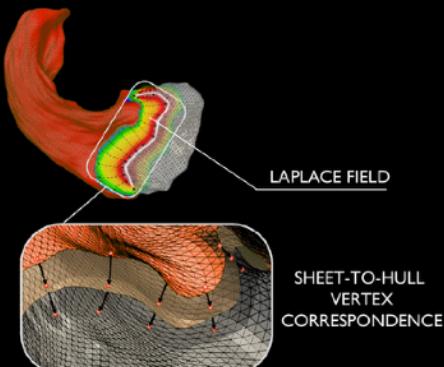
C SPHARDM-PDM PARAMETRIZATION OF OUTER HULL



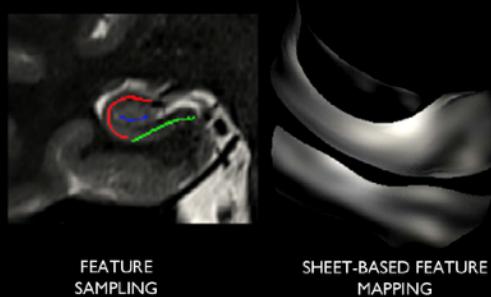
D GENERATION OF MEDIAL SHEET



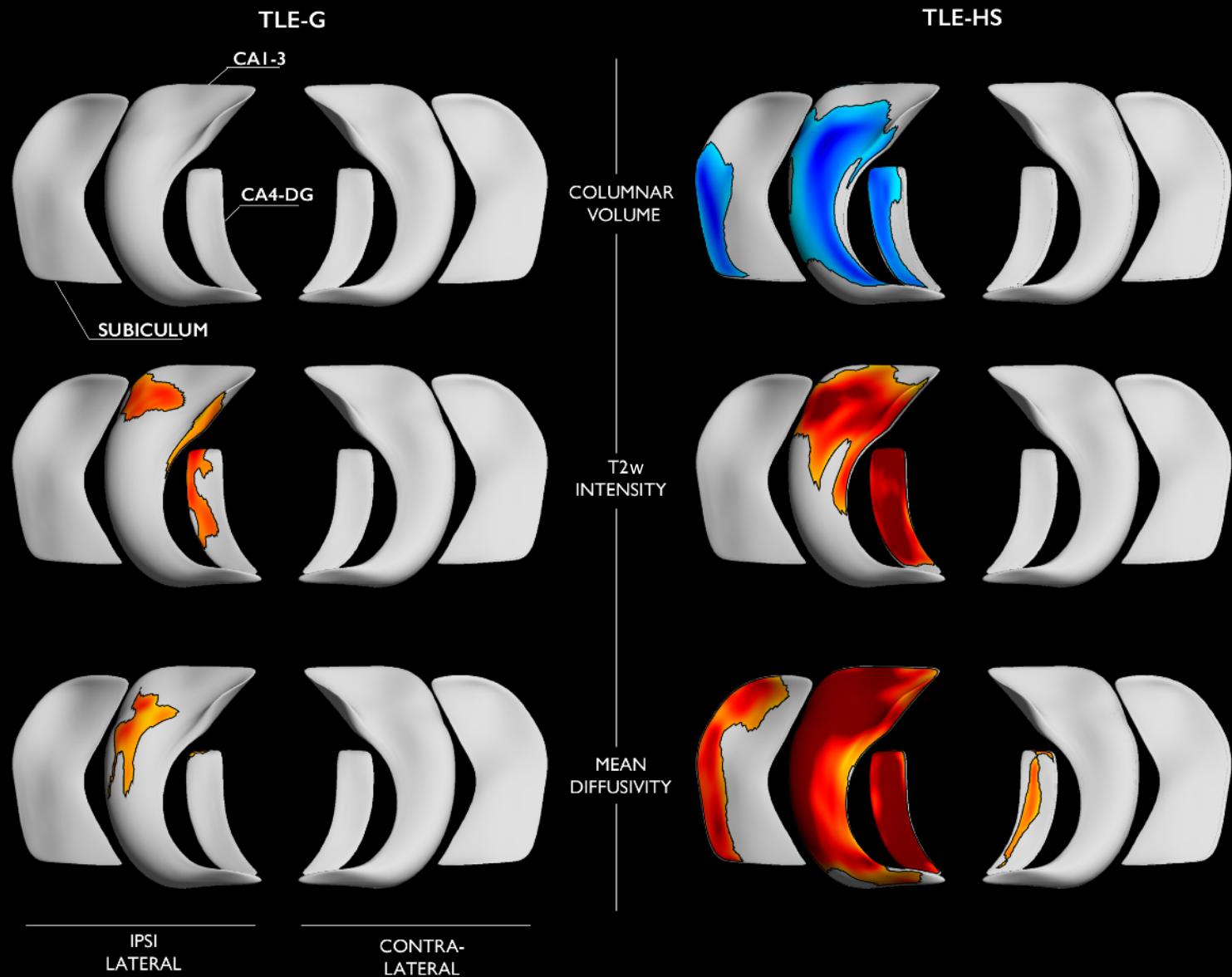
E PROPAGATING PARAMETRIZATION TO SHEET



F SHEET-BASED MEASURES

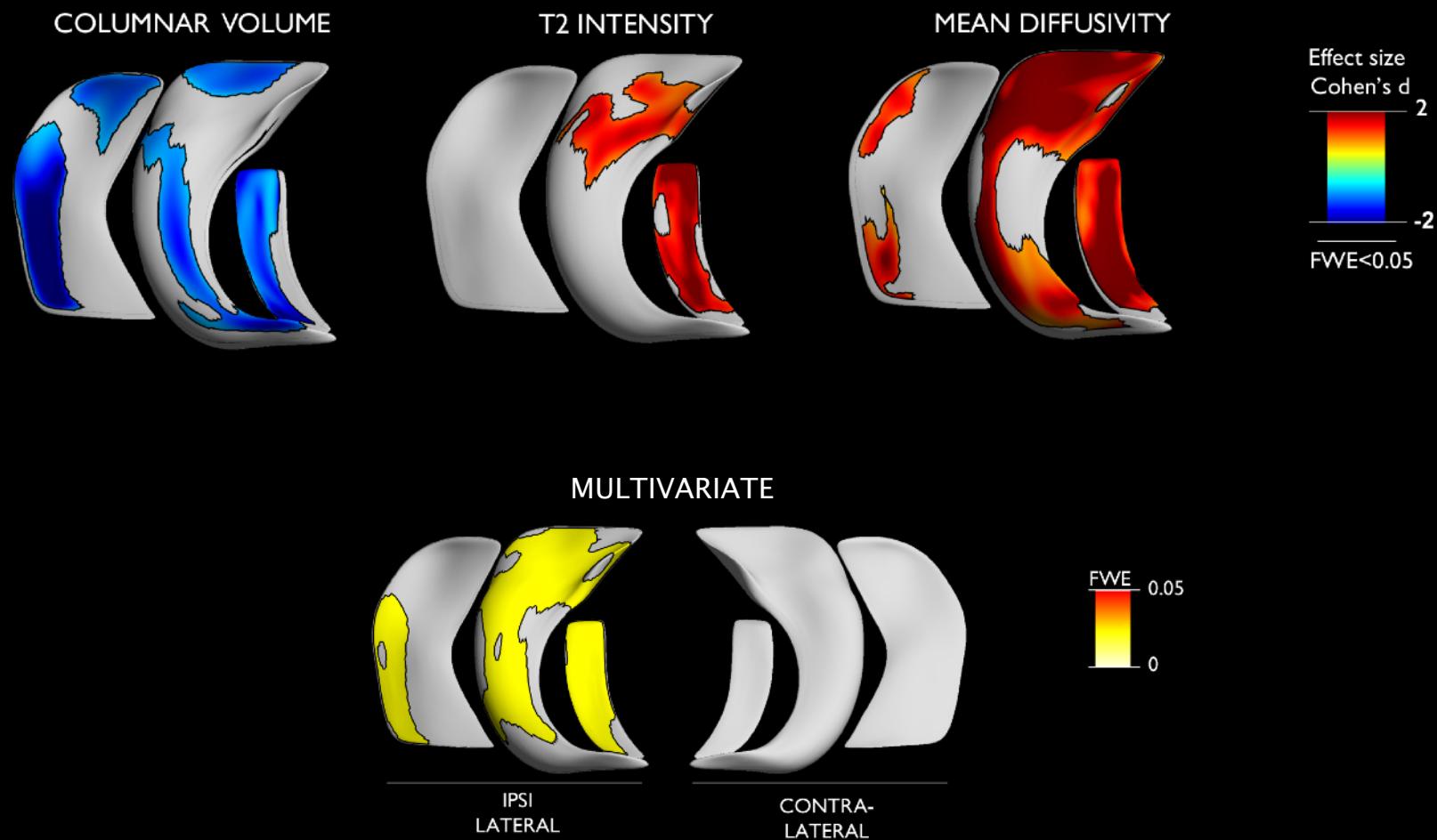


FEATURE-SPECIFIC COMPARISON TO CONTROLS



DIRECT CONTRASTS

B DIRECT CONTRAST: TLE-HS vs TLE-G

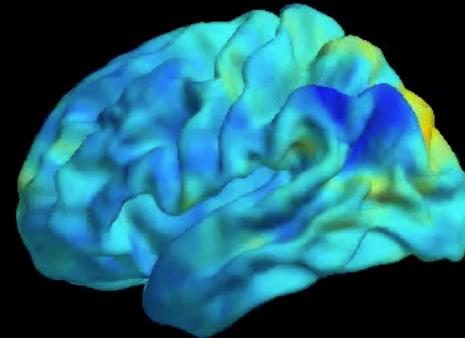


FUNCTION

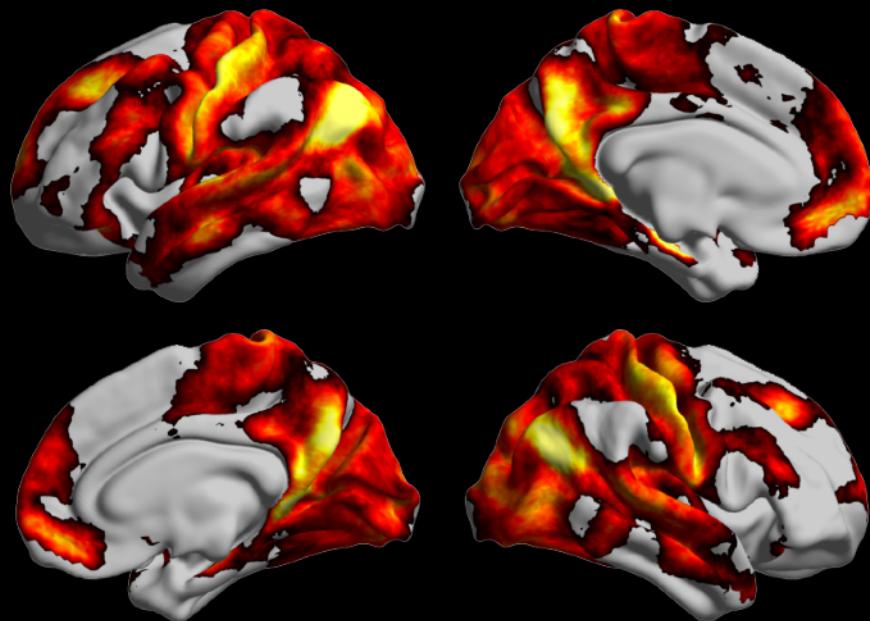
rs-FMRI ANALYSIS OF
INTRINSIC FUNCTIONAL NETWORKS

HIPPOCAMPUS HIGHLY INTEGRATED
WITH DMN

TLE-HS vs TLE-G:
DISEASE MODEL TO PROBE
STRUCTURE-FUNCTION RELATIONS



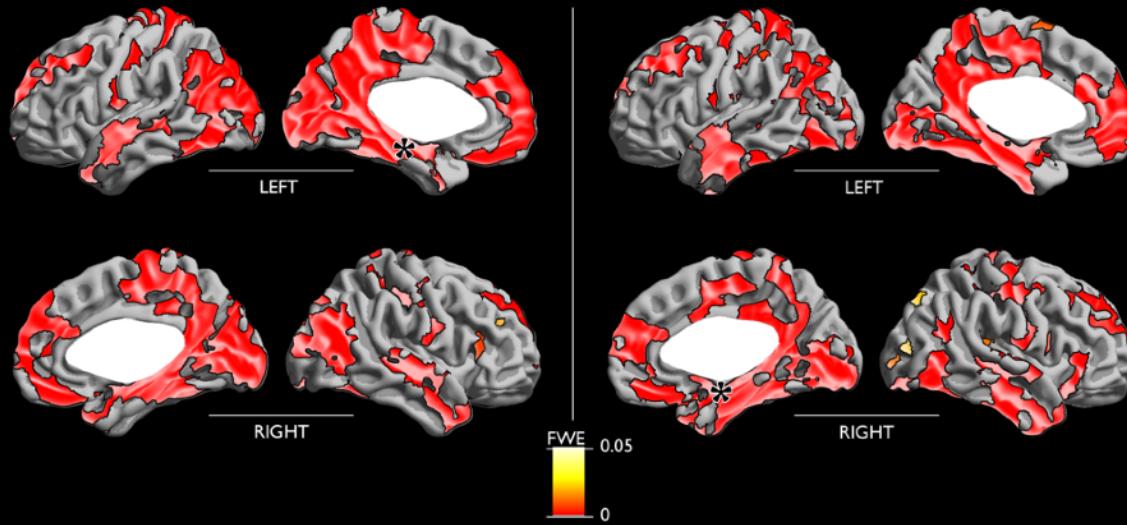
Brain at rest



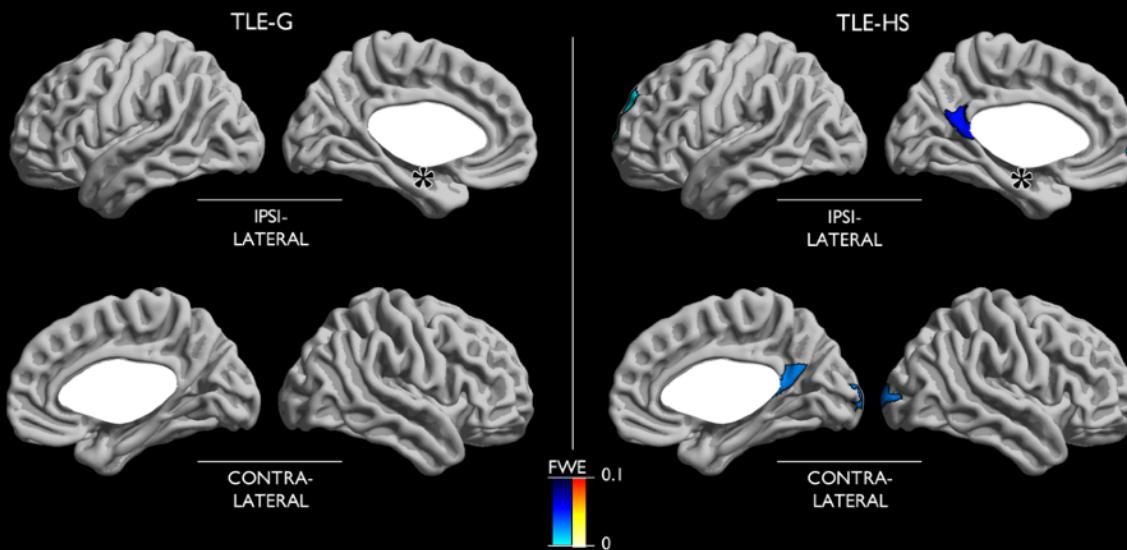
HCP hippocampal connectivity

FUNCTIONAL ANOMALIES IN TLE

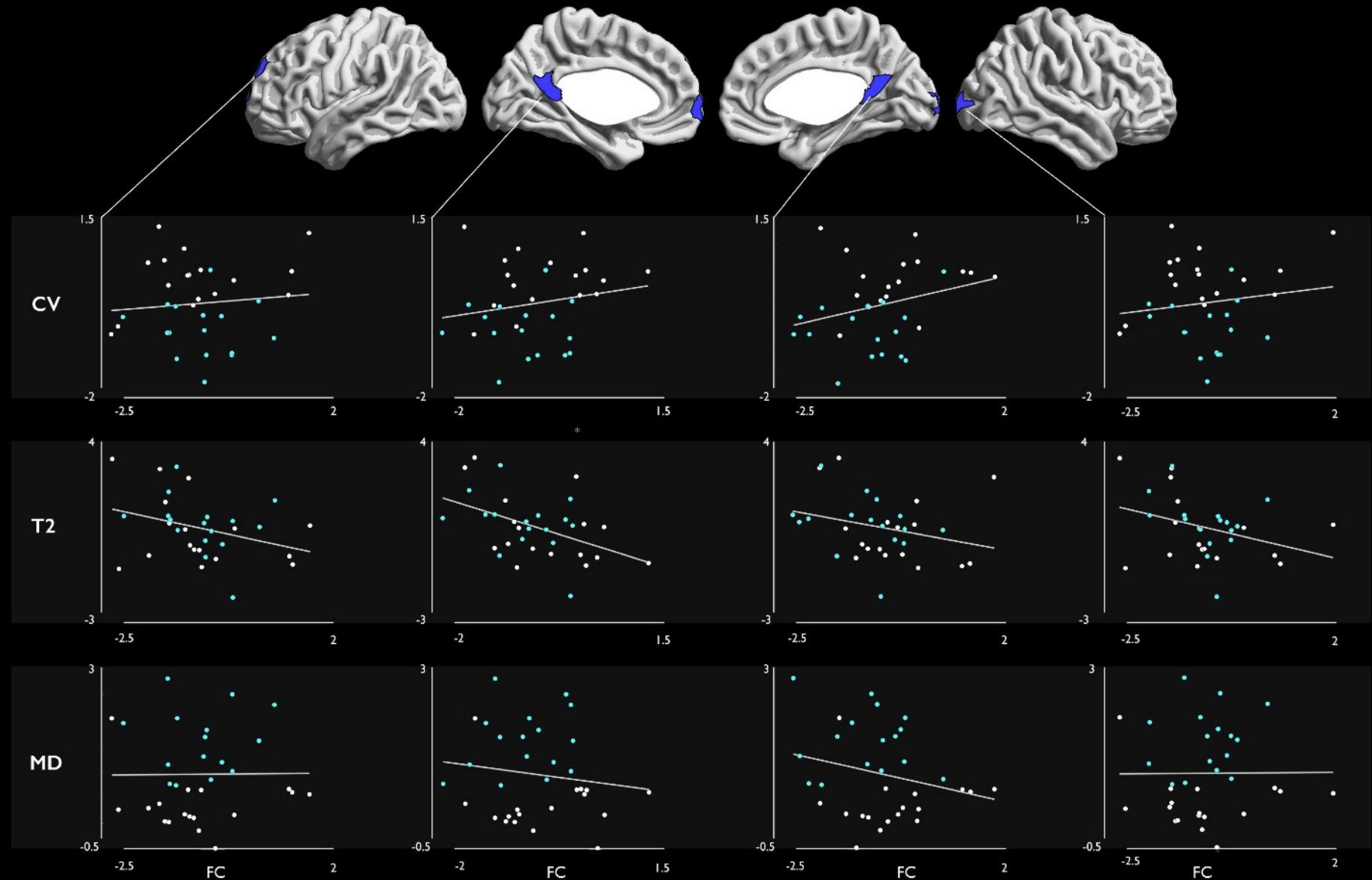
A CONNECTIVITY IN CONTROLS

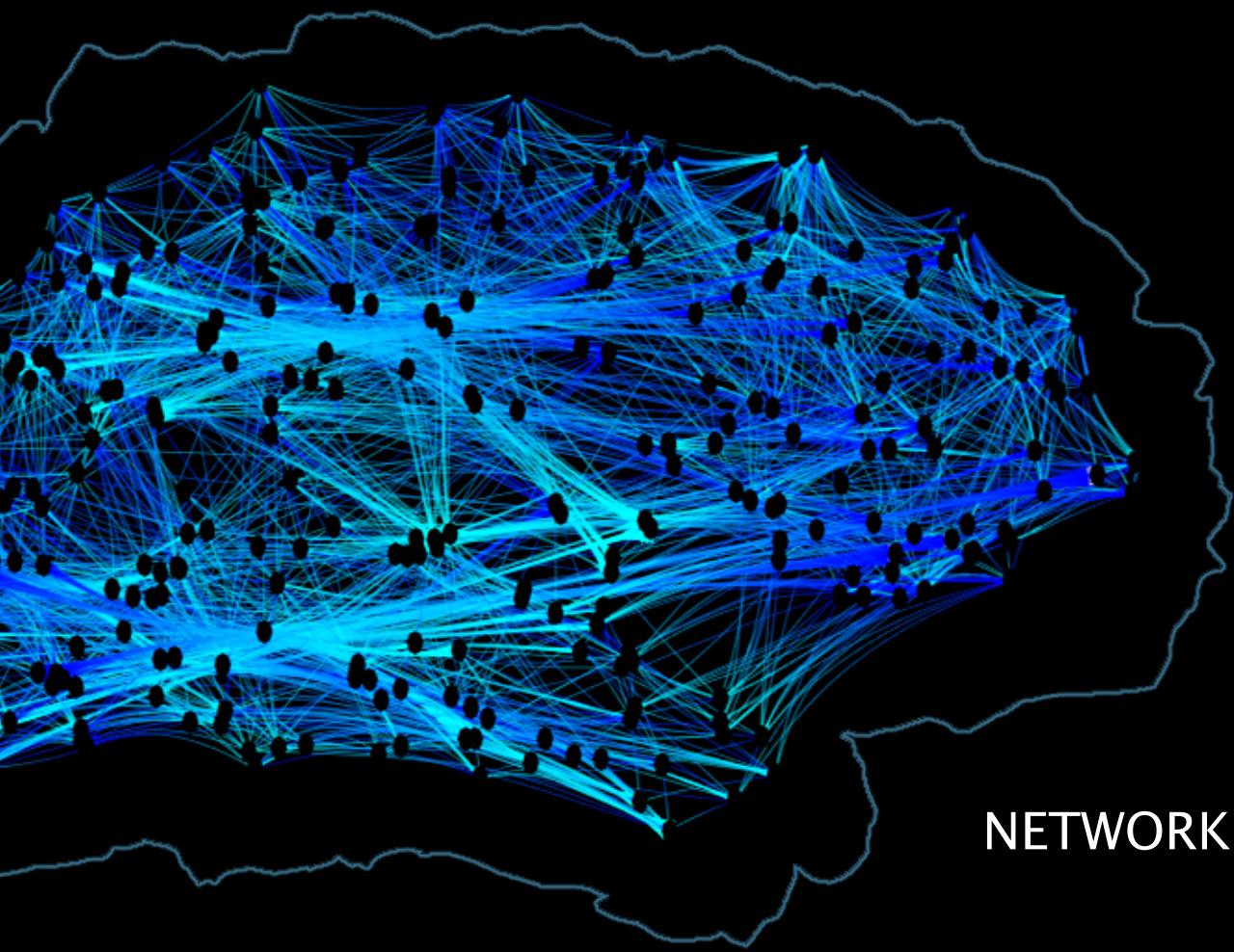


B CONNECTIVITY ALTERATIONS IN TLE

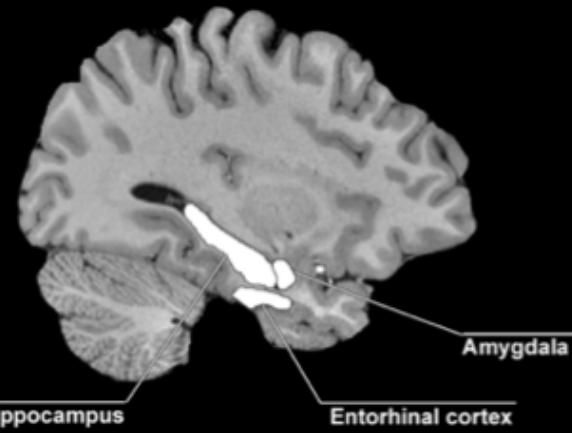


STRUCTURE-FUNCTION RELATIONSHIPS IN TLE

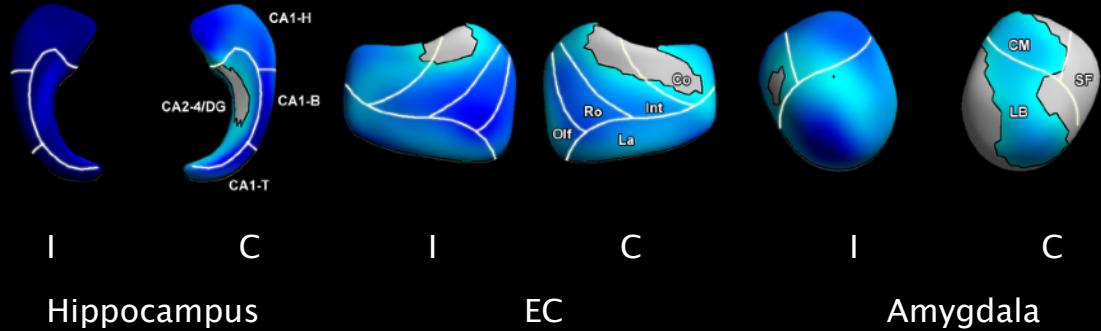




NETWORK LEVEL COMPROMISE IN TLE



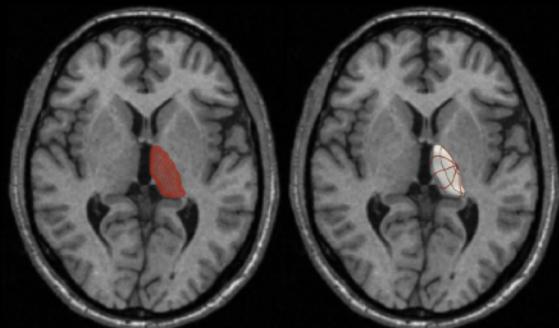
MTL



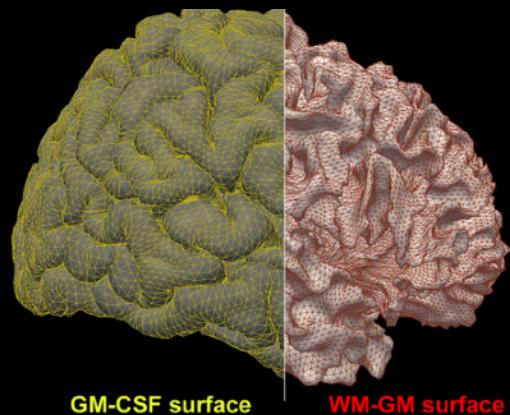
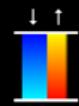
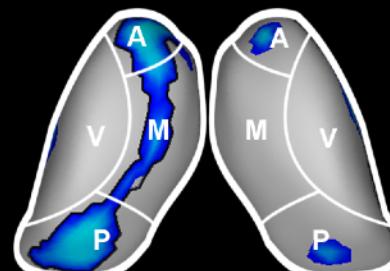
Hippocampus

EC

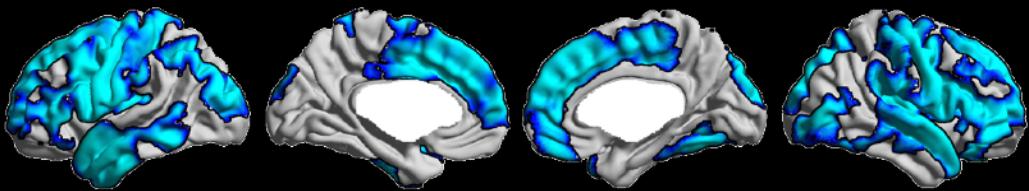
Amygdala

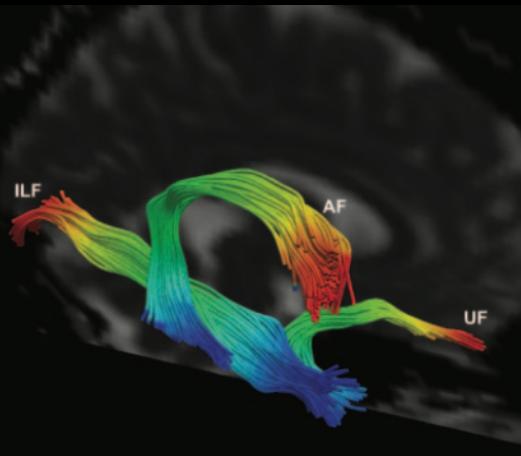


THALAMUS

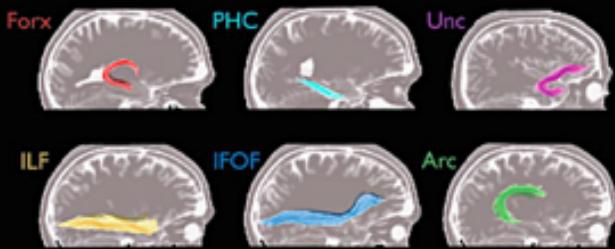


NEOCORTEX

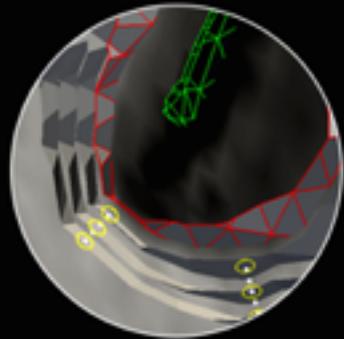




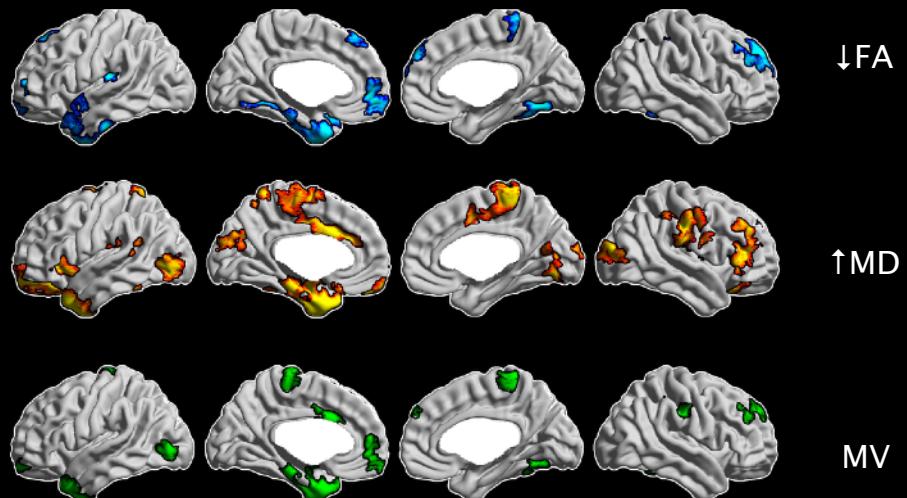
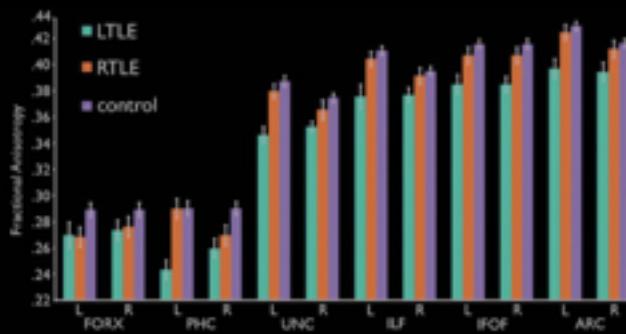
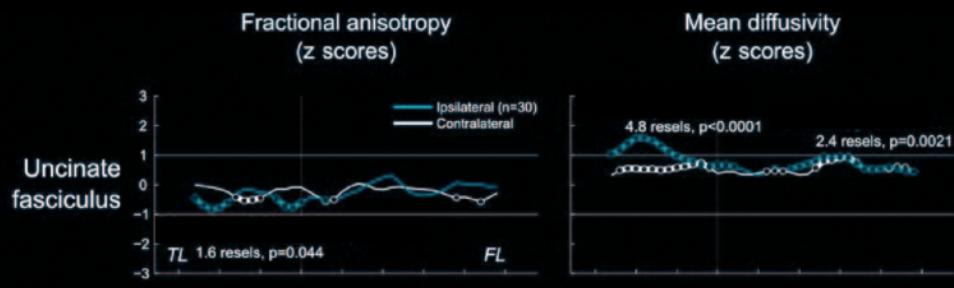
INDIVIDUAL BUNDLES



MULTIPLE TRACTS

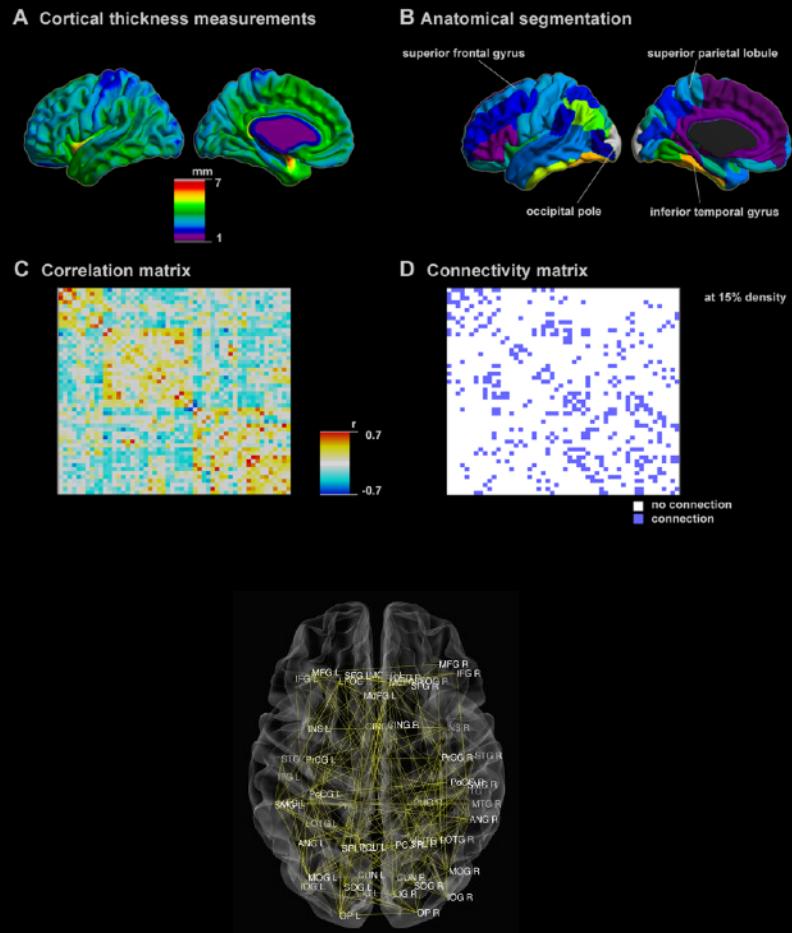


SUPERFICIAL WM

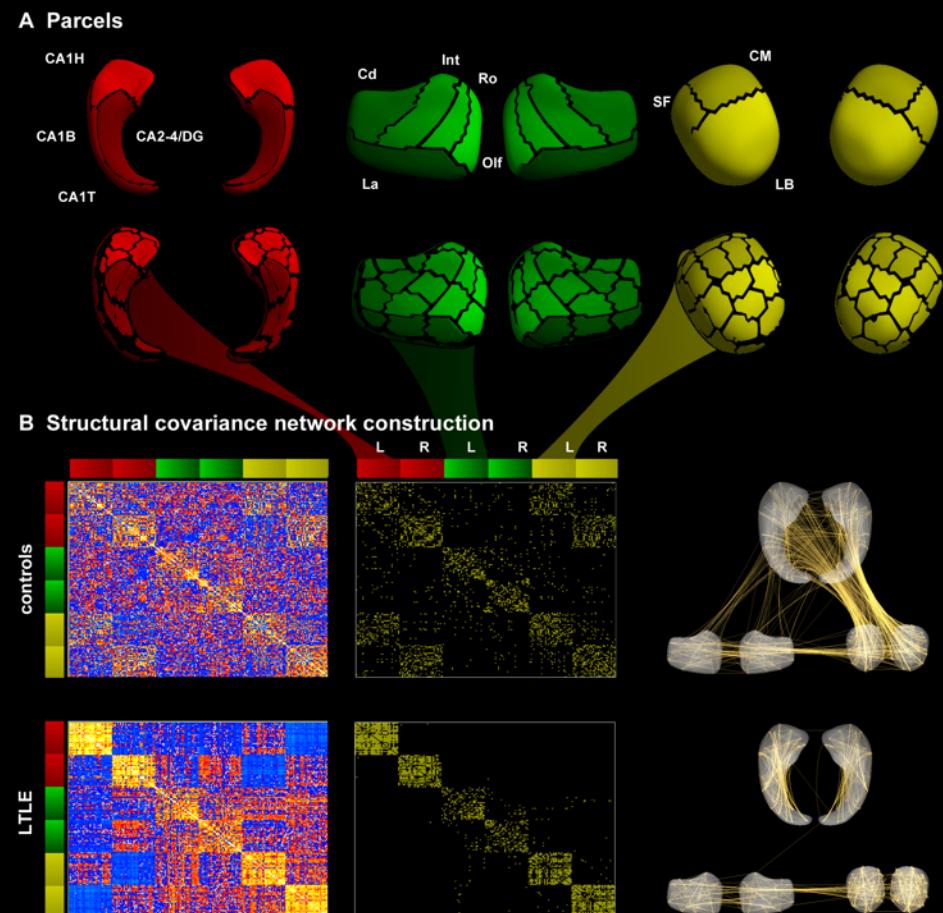


MACROLEVEL STRUCTURAL NETWORK GENERATION

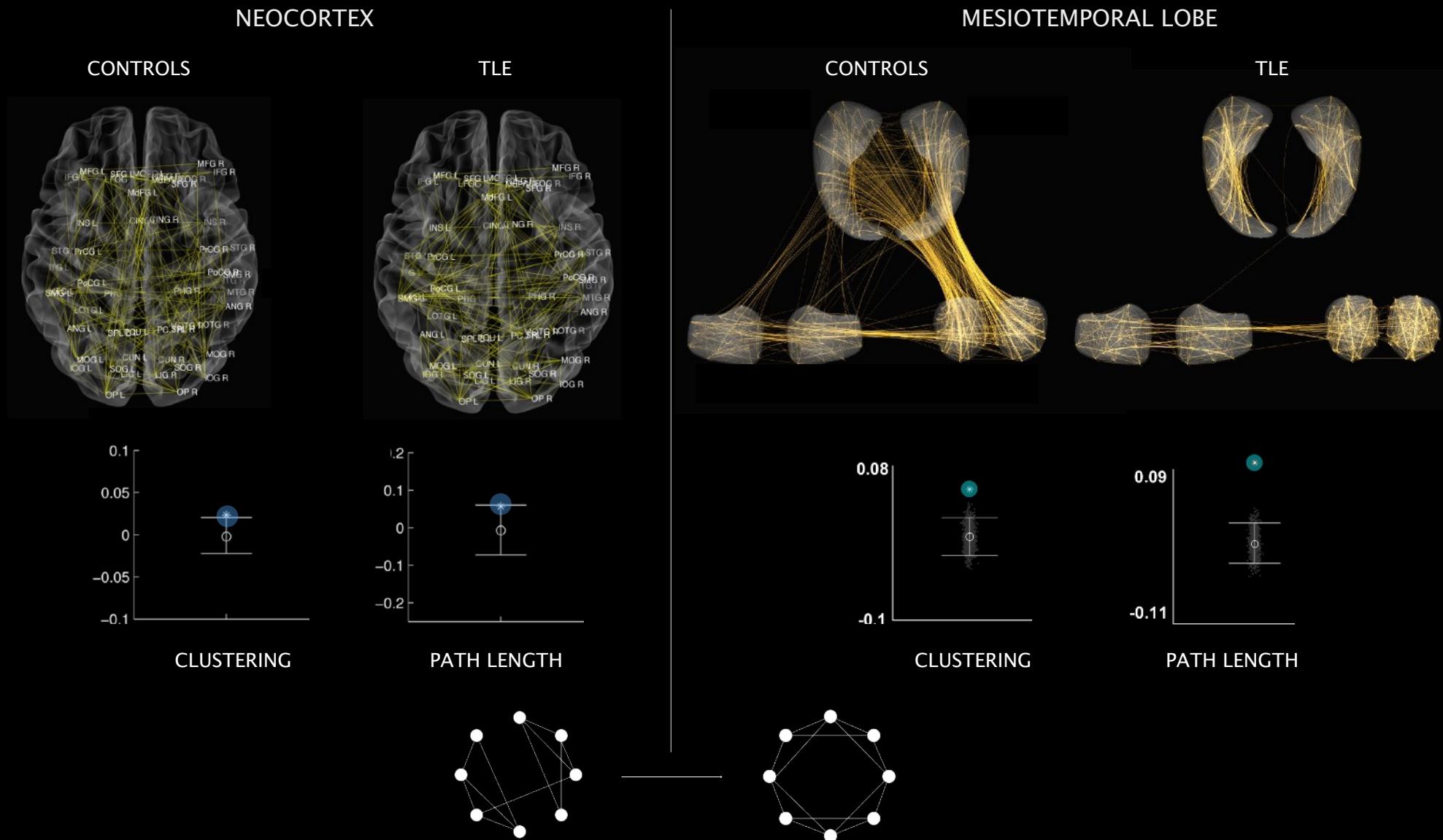
NEOCORTEX



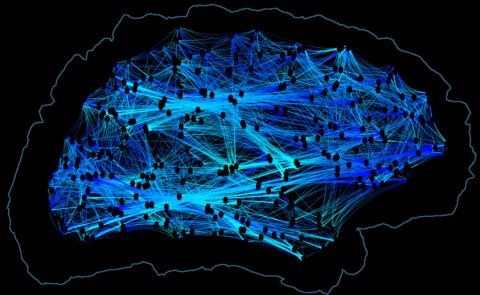
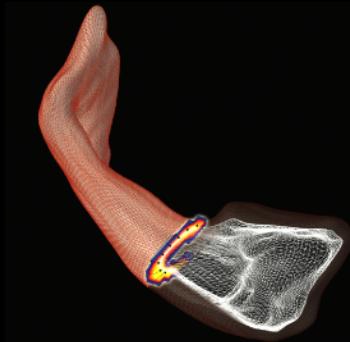
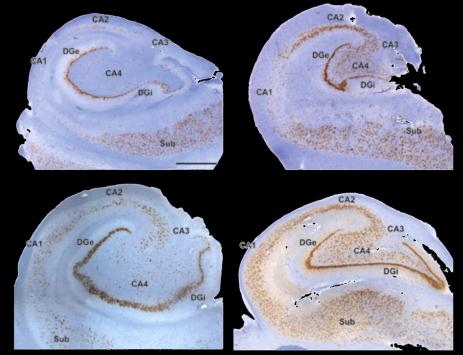
MESIOTEMPORAL LOBE



MACROLEVEL STRUCTURAL NETWORK ALTERATIONS

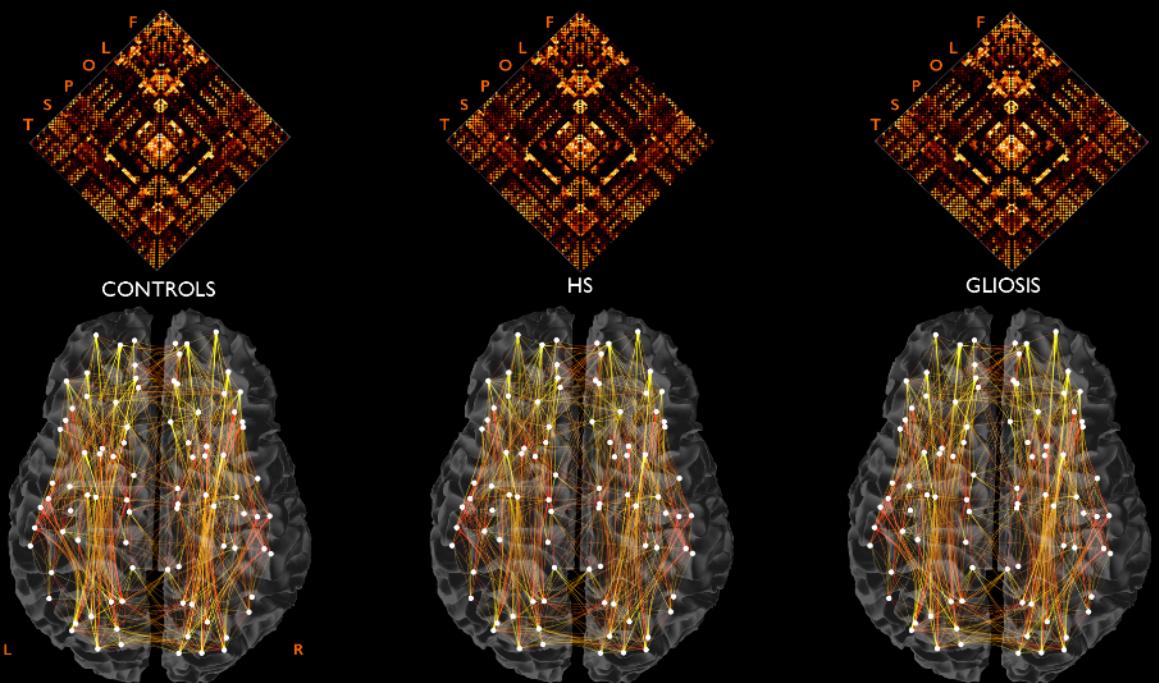


MICRO-MACRO-INTERACTIONS

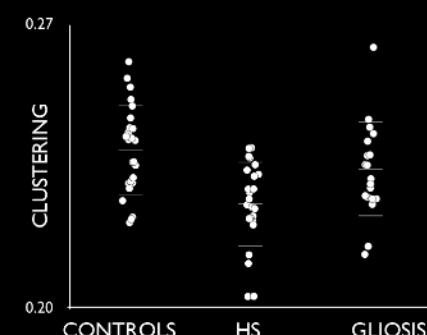
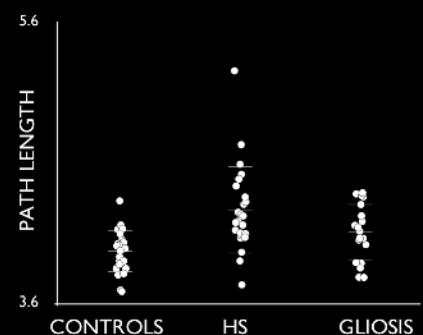


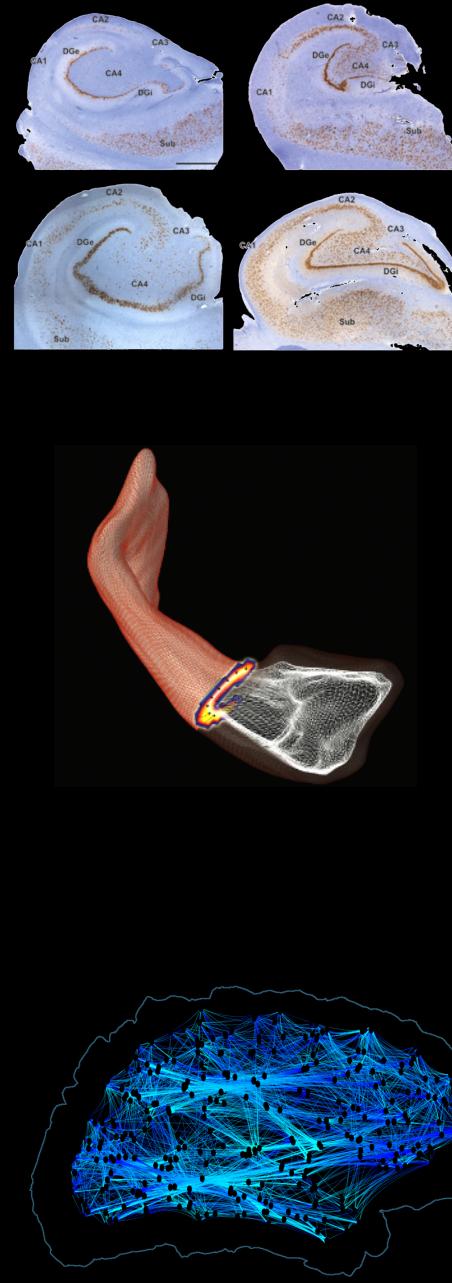
LINKING MACRO/MICROLEVEL DISRUPTIONS

A STRUCTURAL CONNECTOMES



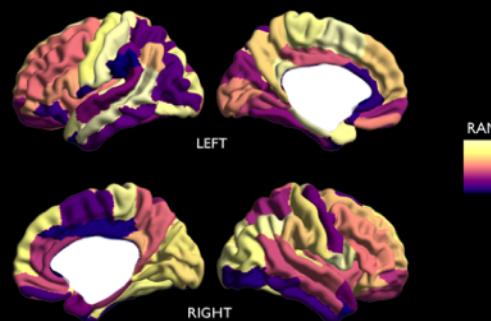
B TOPOLOGICAL PARAMETER ANALYSIS



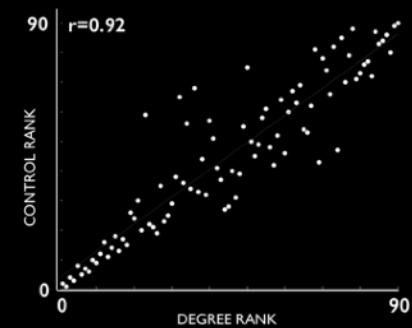


LINKING MACRO/MICROLEVEL DISRUPTIONS

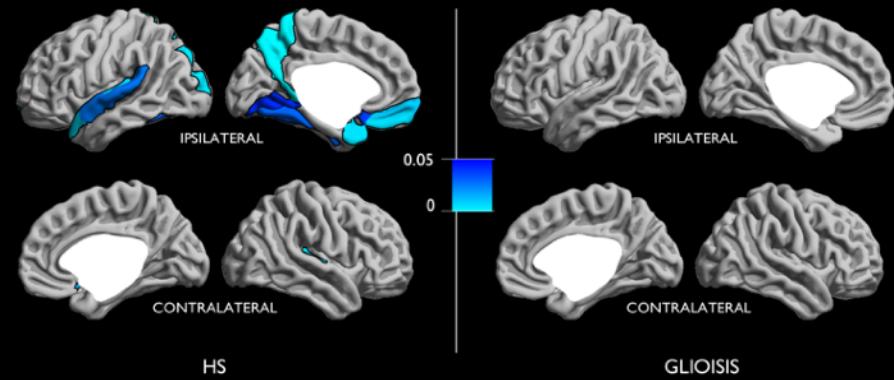
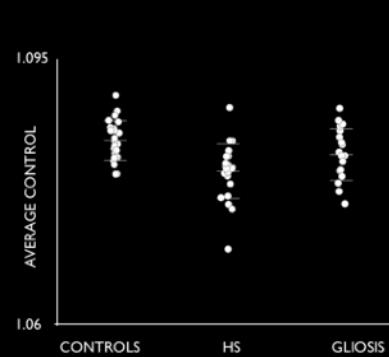
A NETWORK CONTROLLABILITY

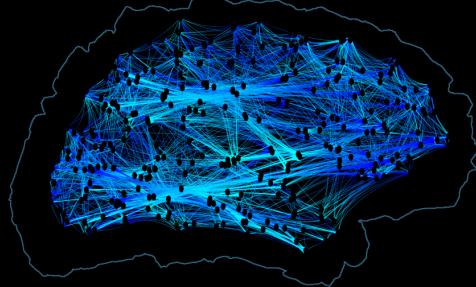
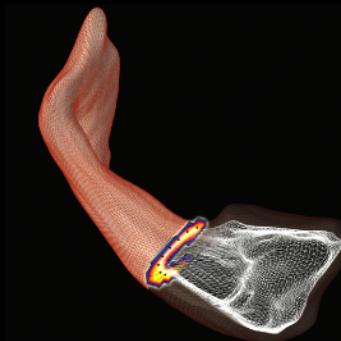
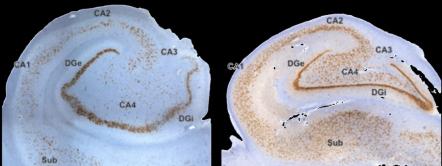
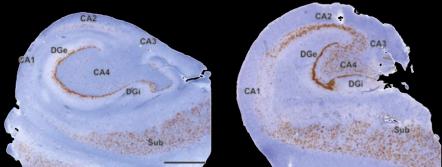


B RELATION TO CENTRALITY



C CONTROLLABILITY ALTERATIONS IN TLE



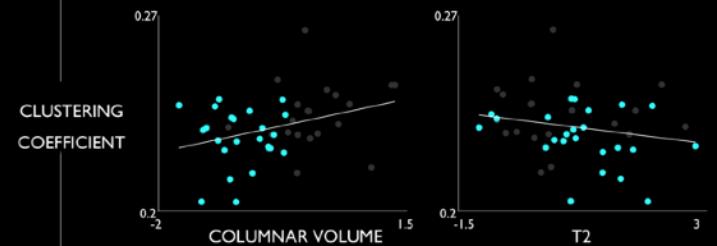


LINKING MACRO/MICROLEVEL DISRUPTIONS

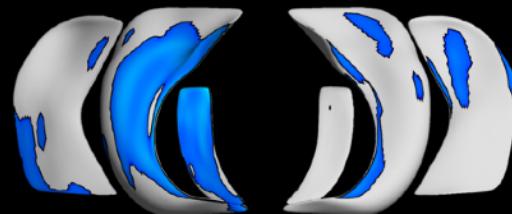
MULTIVARIATE SURFACE-WIDE



UNIVARIATE POSTHOC



PATH LENGTH



AVERAGE
CONTROLABILITY



FDR<0.05

MULTIVARIATE POSTHOC

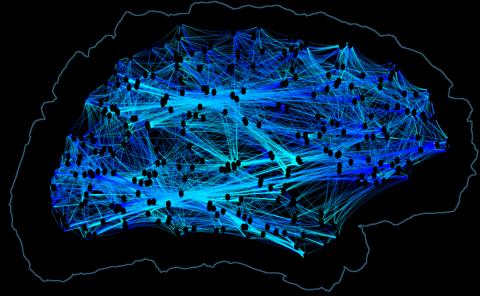
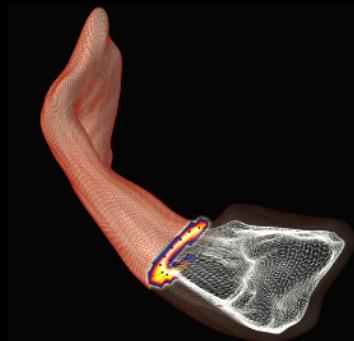
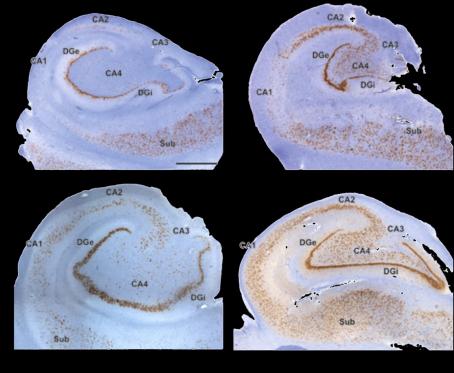


INTERSECTION

CLUSTERING &
PATH LENGTH &
CONTROLLABILITY

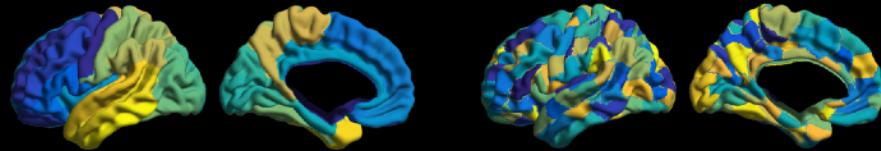


COLUMNAR VOLUME & T2

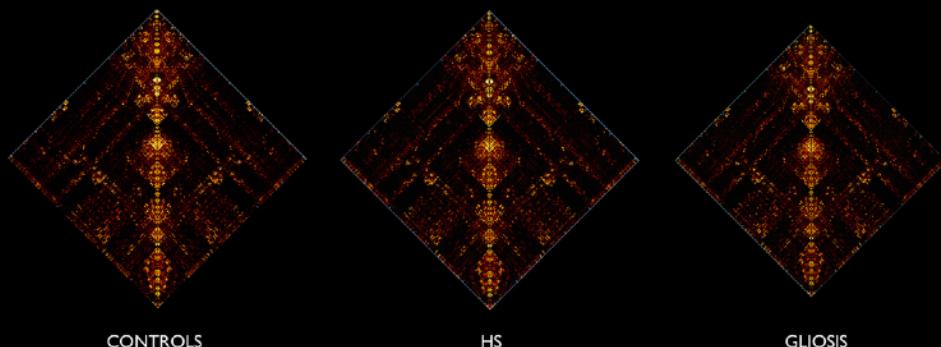


REPRODUCIBILITY AT HIGHER SPATIAL SCALE

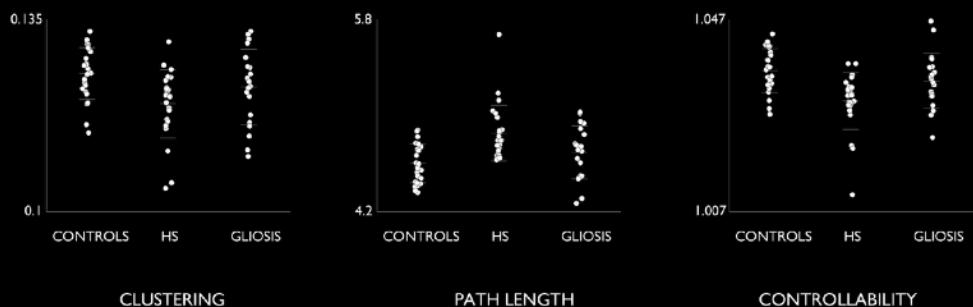
A AAL SUBPARCELLATION



B HIGH-RESOLUTION CONNECTOMES IN CONTROLS AND TLE



C RELATION TO TOPOLOGY AND CONTROLLABILITY



INTERIM SUMMARY: EPILEPSY

MULTIPARAMETER MRI:
IN-VIVO DESCRIPTION OF HS IN TLE

WHOLE-BRAIN STUDIES INDICATE
MARCOLEVEL ANOMALIES BEYOND MTL

HS GRADES NEVERTHELESS CLOSELY
RELATE TO CONNECTOME PHENOTYPES

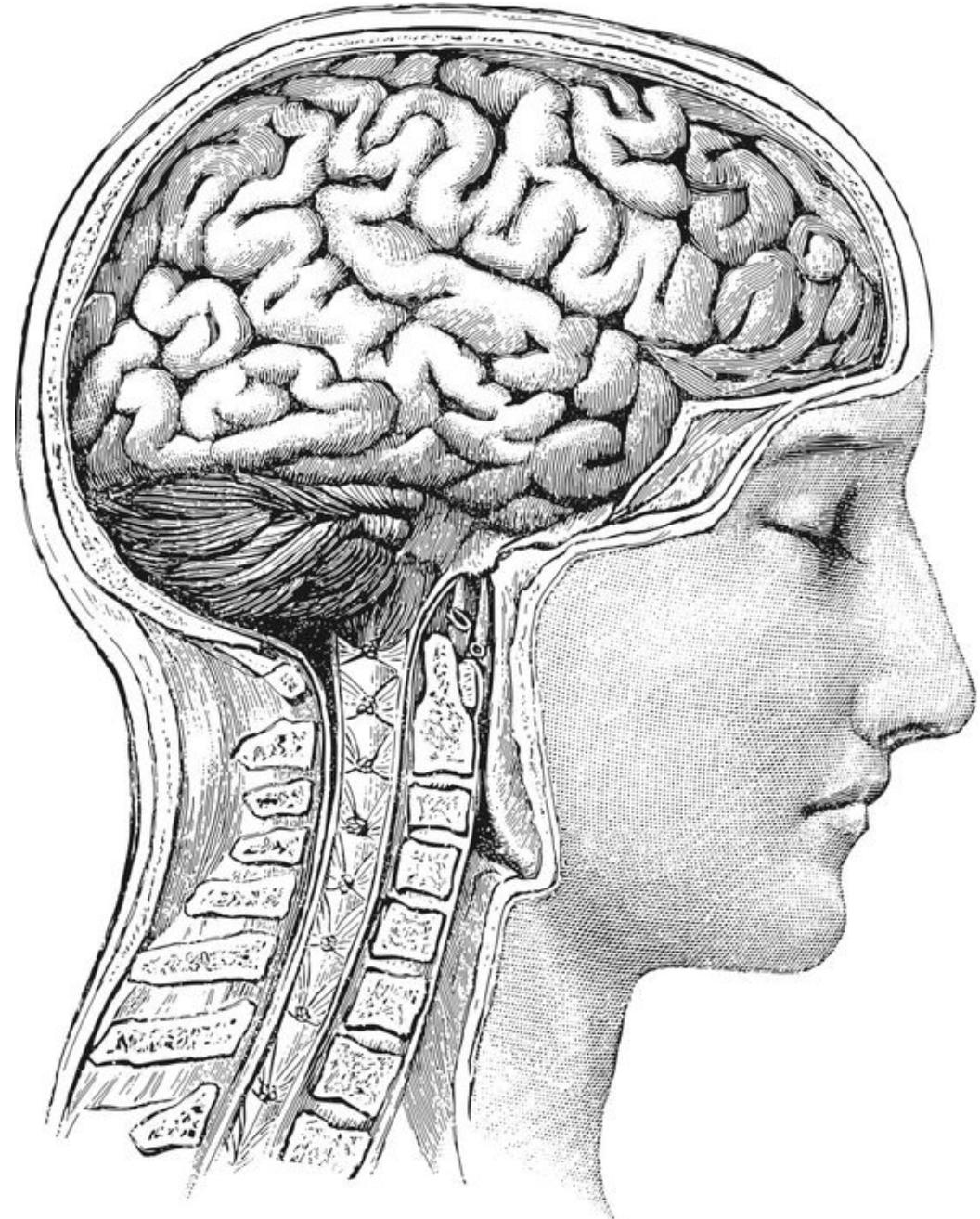
NEUROIMAGING AND CONNFCOMICS
PROMISE TO PROVIDE PROGNOSTIC MARKERS OF
PATHOLOGY AND OUTCOMES

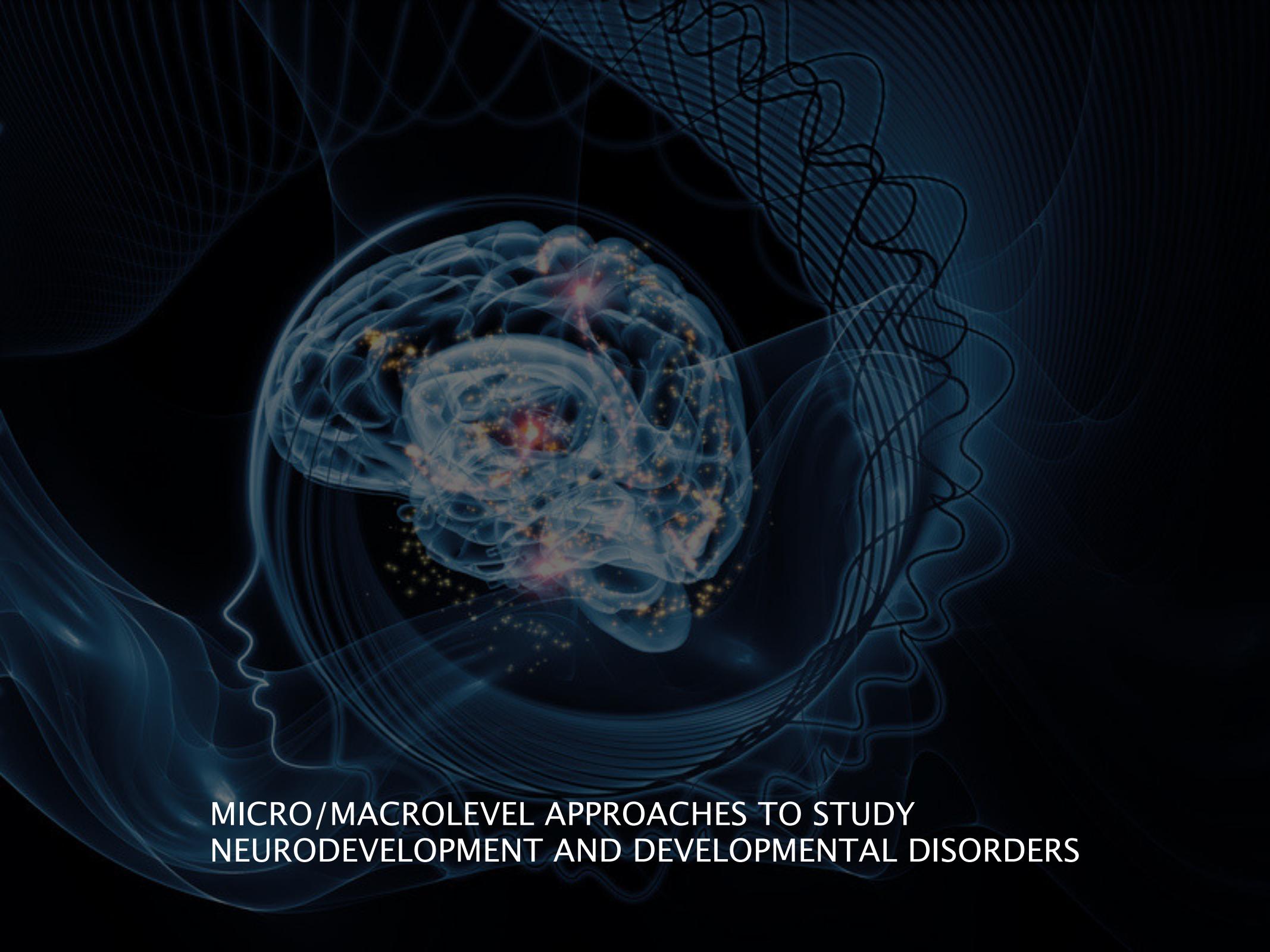
SUMMARY

MRI UNVEILS MICROSTRUCTURE AND
MACROSCALE NETWORKS

STRUCTURE-FUNCTION STUDIES OF
HIPPOCAMPAL NETWORK EMBEDDING

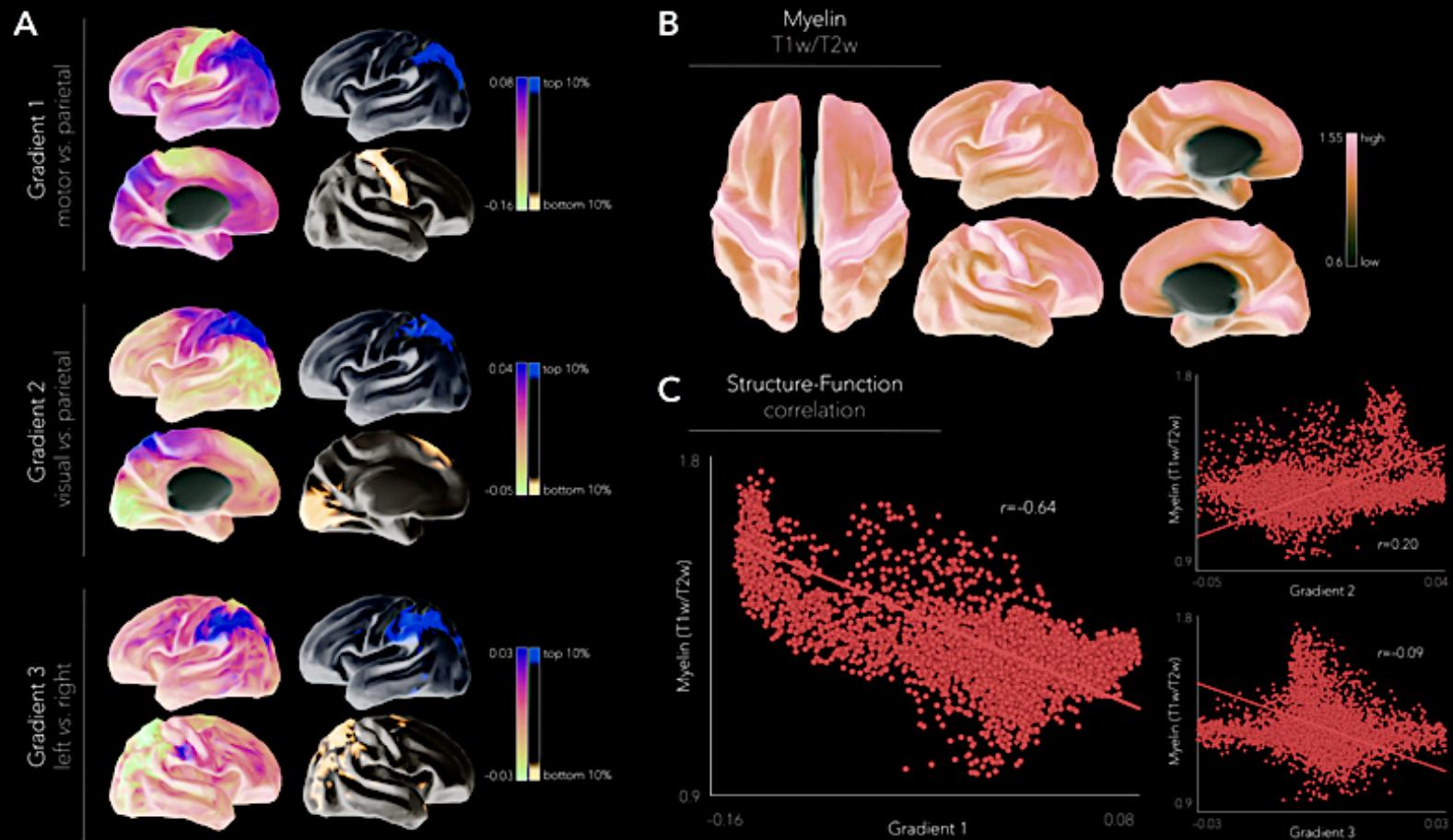
HISTOLOGY, MRI, AND CONNECTOMICS
CHARACTERIZE CAUSAL IMPACT
OF HIPPOCAMPAL LESIONS





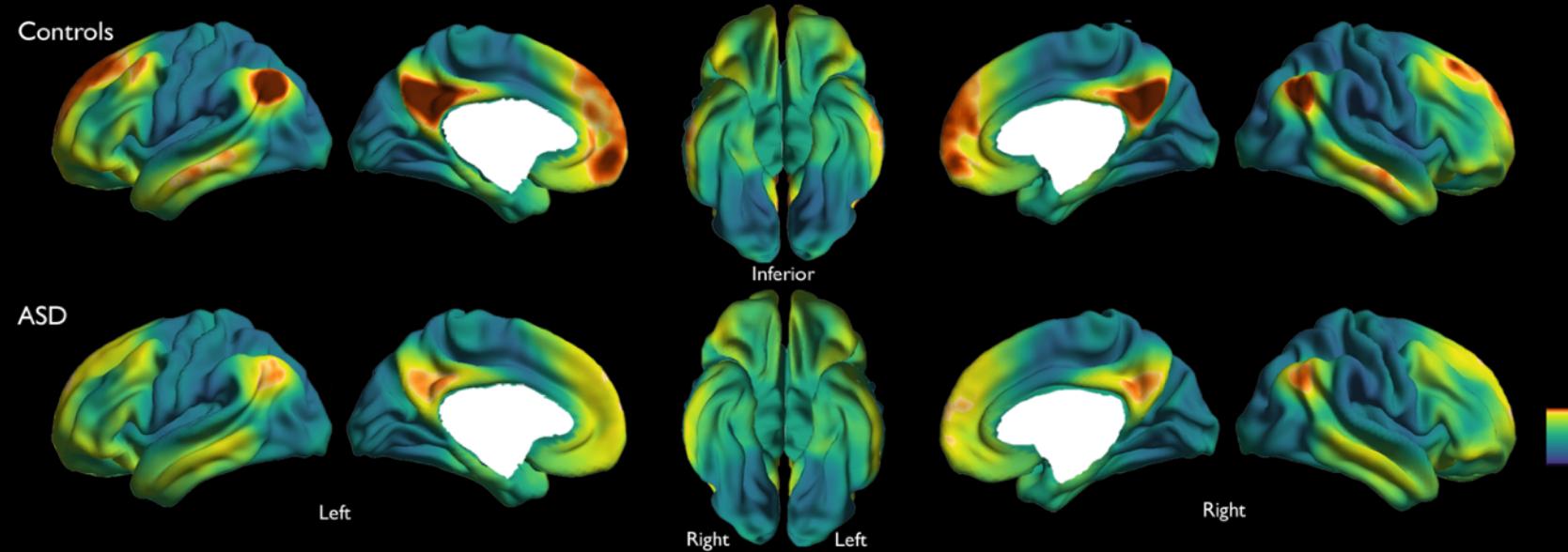
MICRO/MACROLEVEL APPROACHES TO STUDY
NEURODEVELOPMENT AND DEVELOPMENTAL DISORDERS

GRADIENTS IN DEVELOPMENT

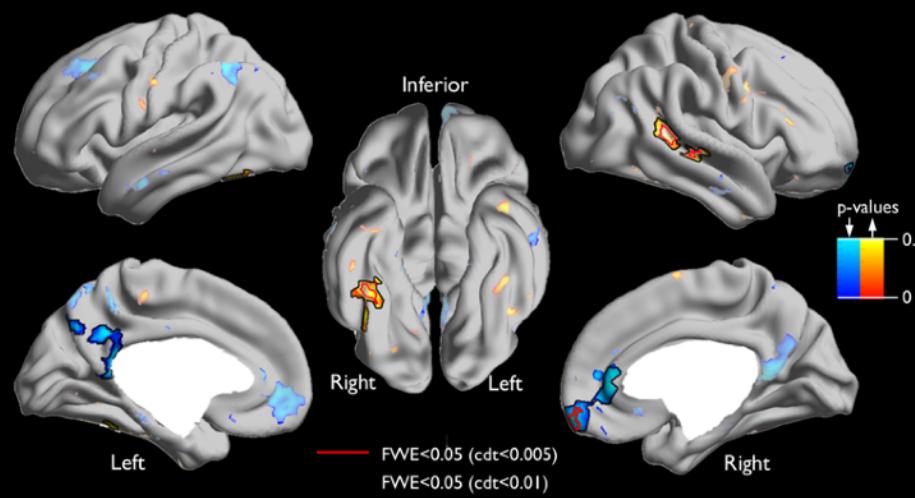


ALTERED CONNECTOME ORGANIZATION IN AUTISM

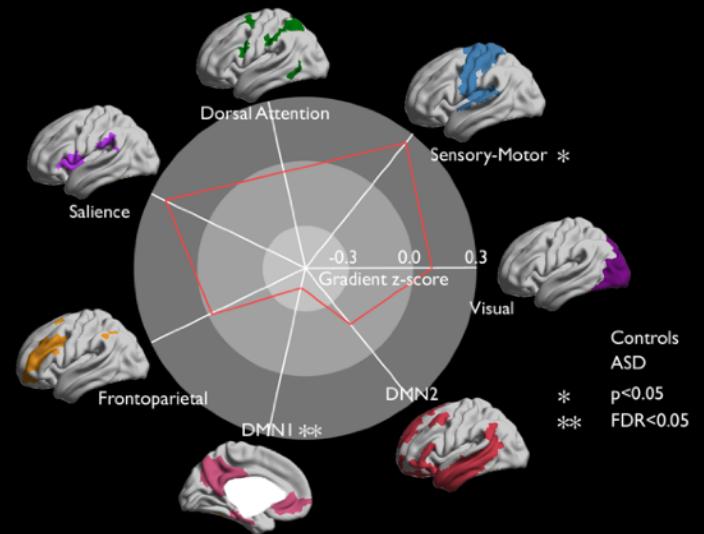
A. Group-averaged functional gradient map



B. Alterations in ASD

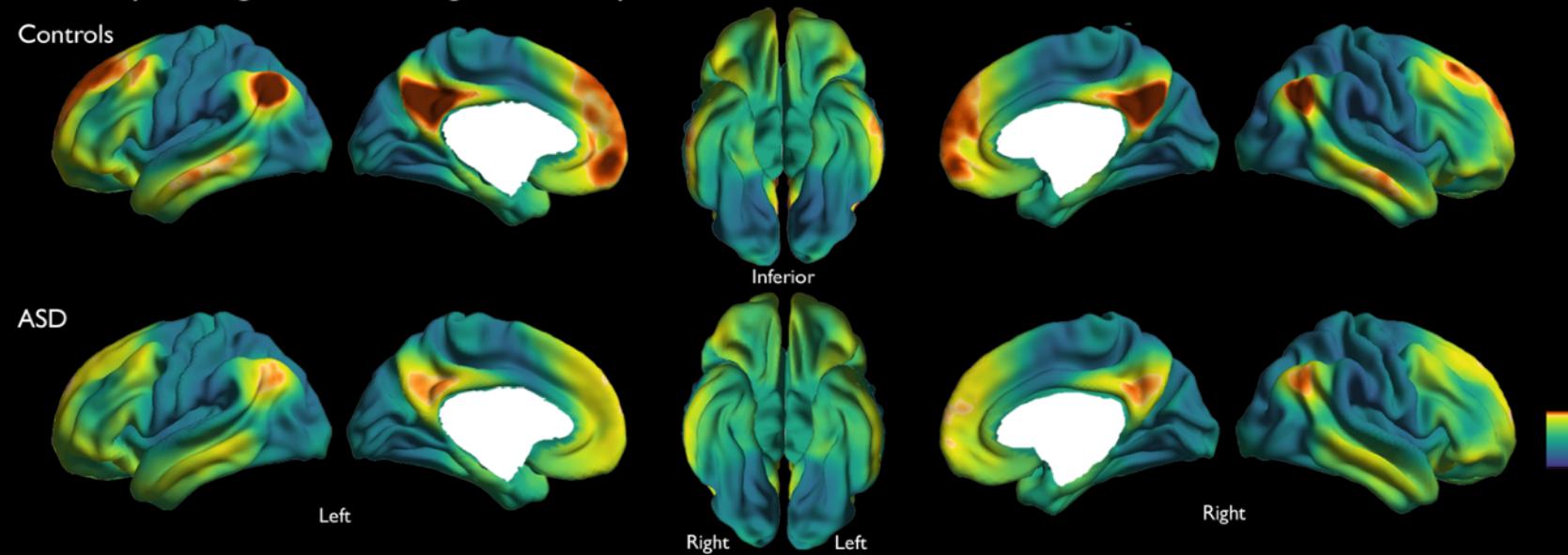


C. Profiling based on functional organization

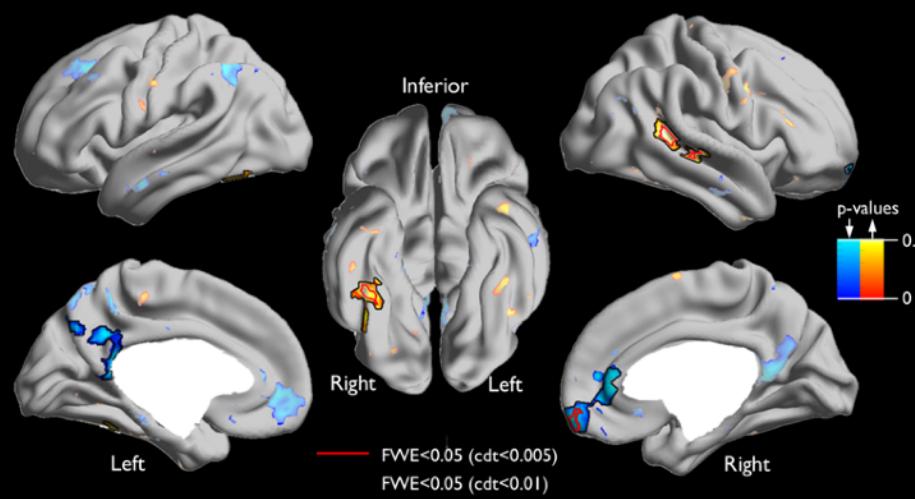


ALTERED CONNECTOME ORGANIZATION IN AUTISM

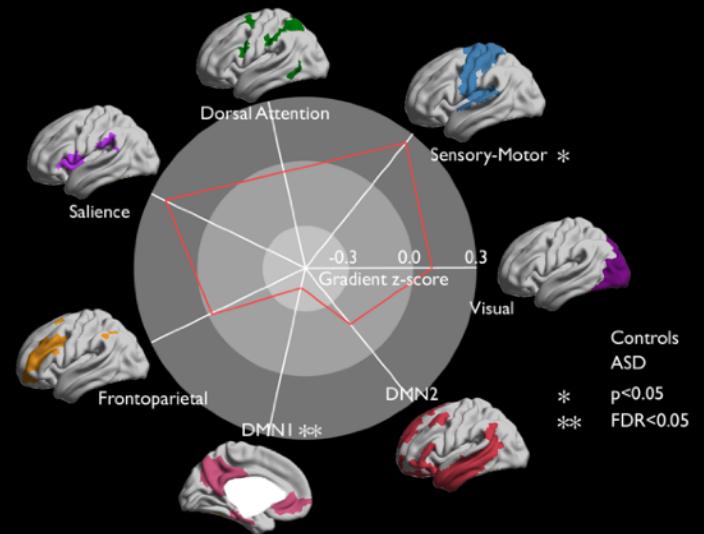
A. Group-averaged functional gradient map



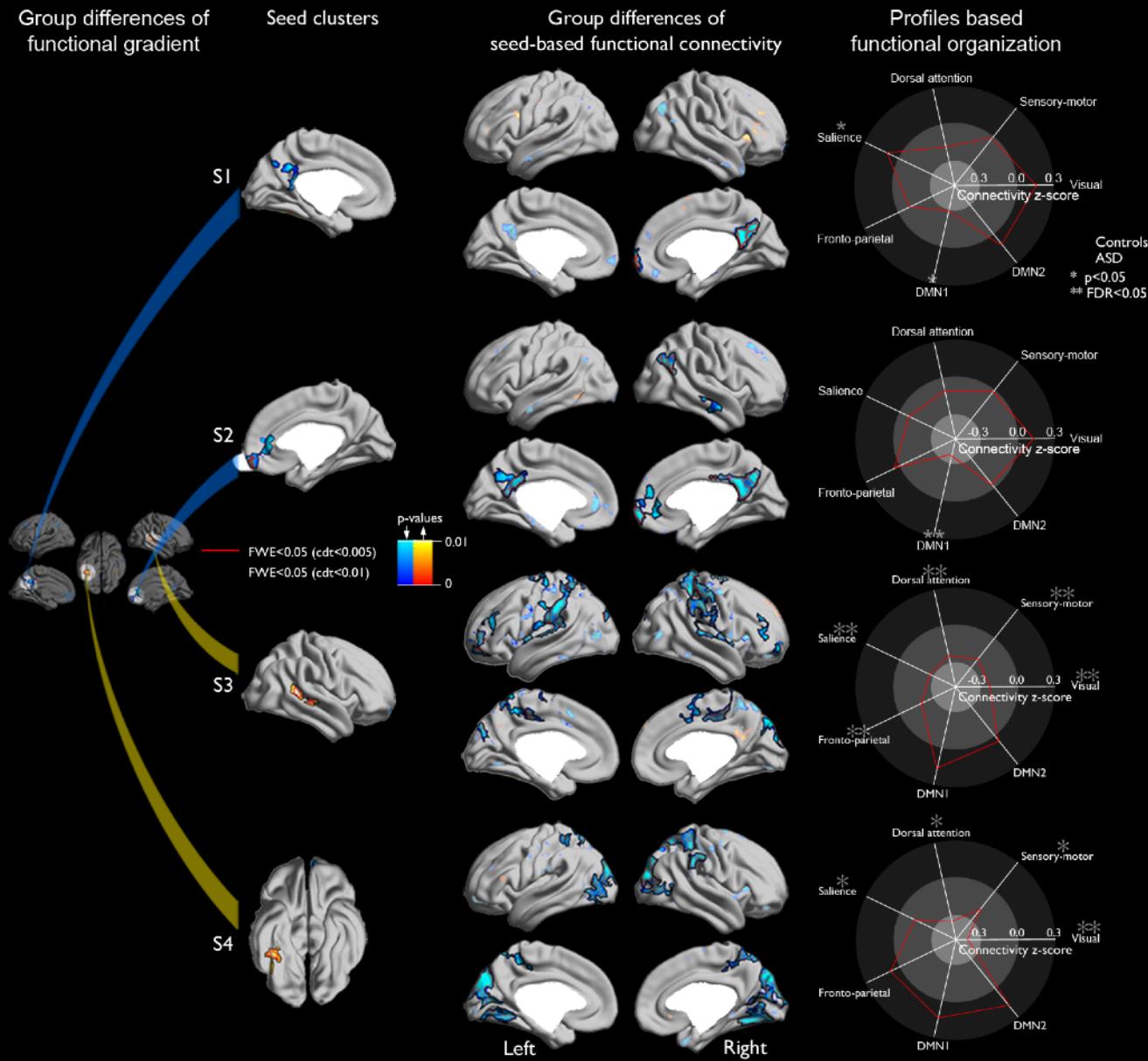
B. Alterations in ASD



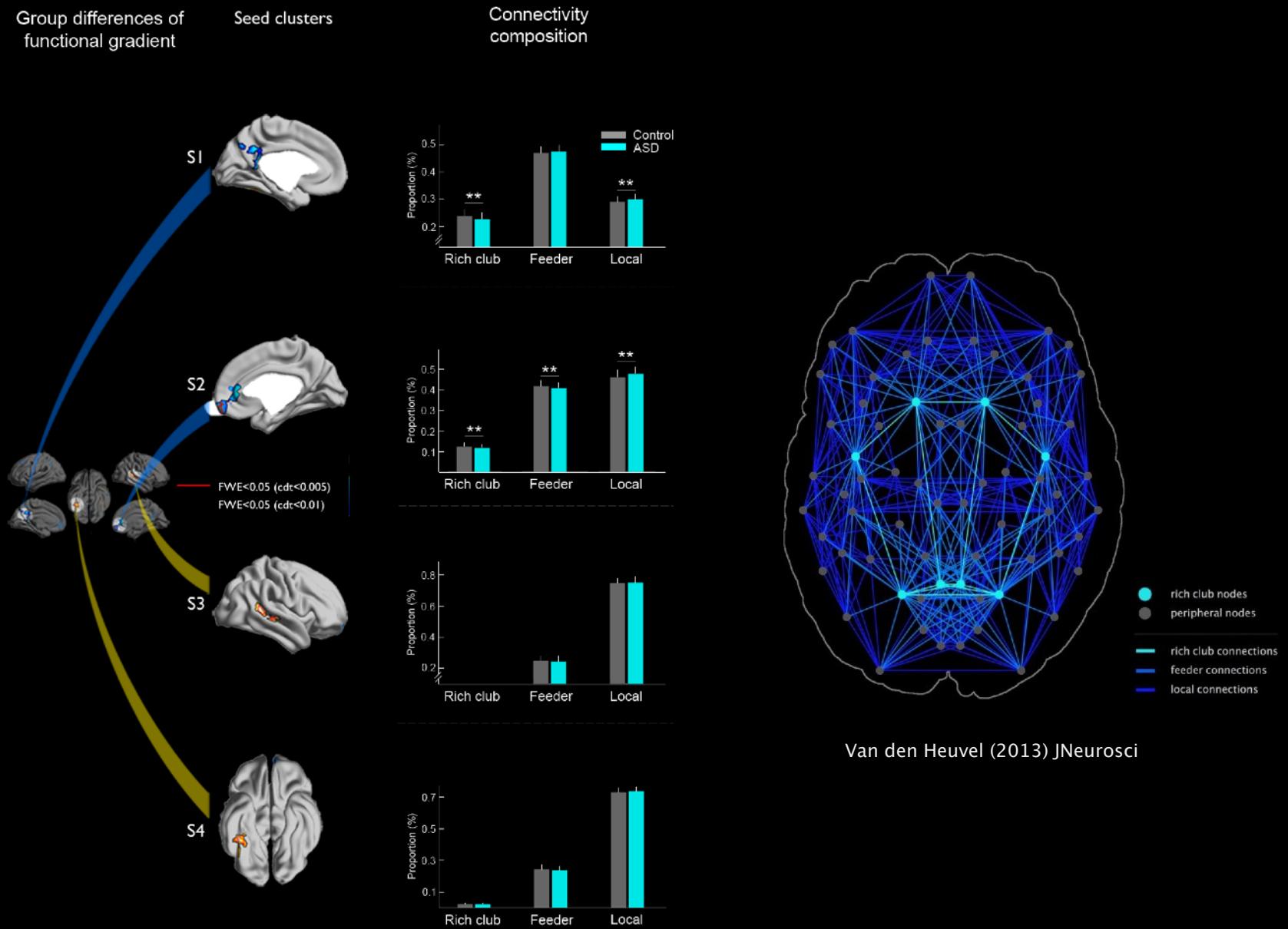
C. Profiling based on functional organization



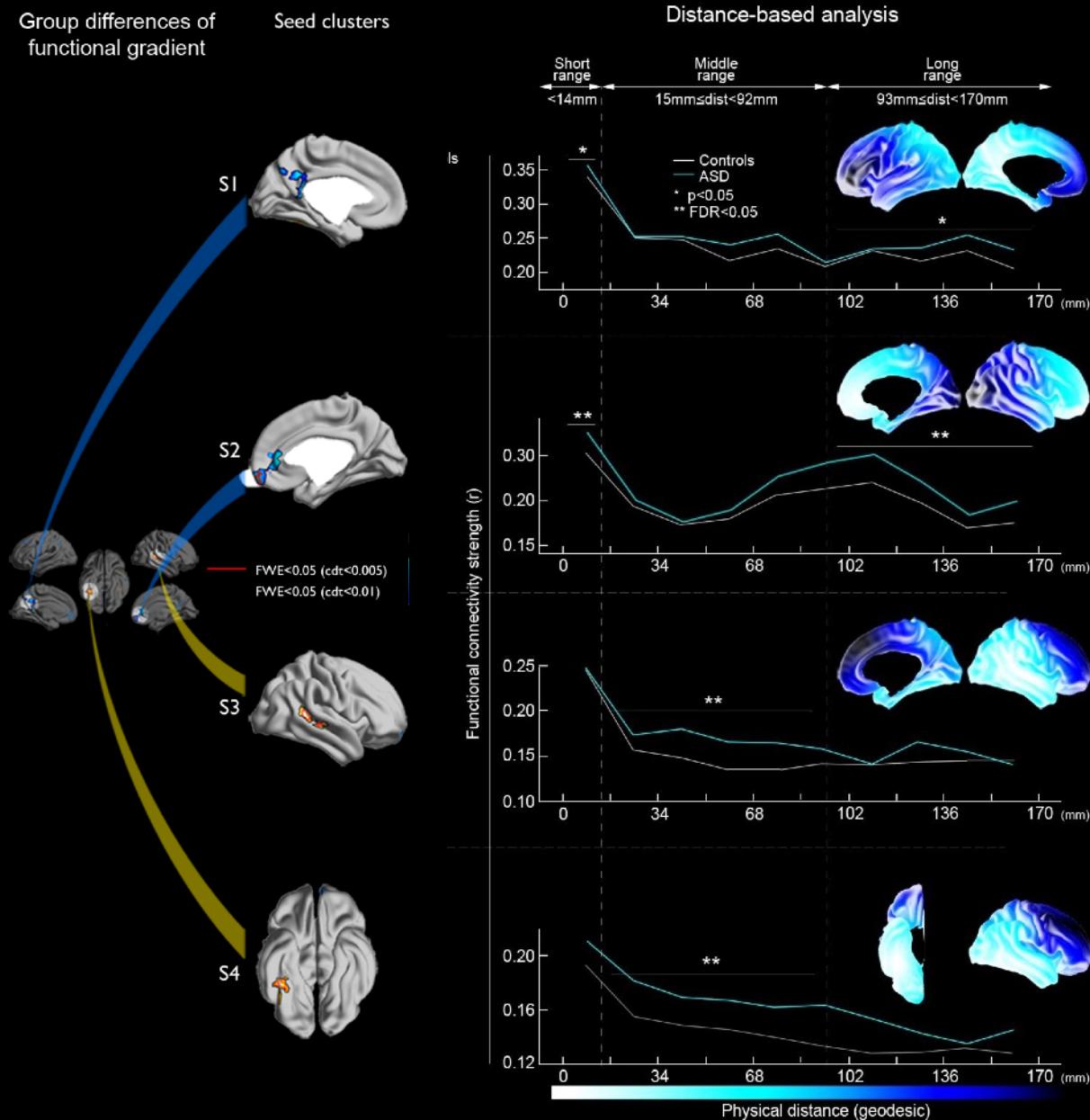
ALTERED CONNECTOME ORGANIZATION IN AUTISM



ALTERED CONNECTOME ORGANIZATION IN AUTISM



ALTERED CONNECTOME ORGANIZATION IN AUTISM





Neda Bernasconi
Andrea Bernasconi
Jessie Kulaga Yoskovitz

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Sofie Valk

Tania Singer

Alfred Anwander

Daniel Margulies



Together We Will.



Luis Concha
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