



FROM MICROSTRUCTURE TO MACROSCALE: NEUROIMAGING AND CONNECTOMICS OF EPILEPSY AND AUTISM

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EPILEPSY AND AUTISM

HIGHLY COMMON DISORDERS

EARLY ONSET

PERSIST INTO ADULTHOOD

SYMPTOMATICALLY DIAGNOSED

HIGH HETEROGENEITY

TREATMENT NOT OPTIMAL



OPTIMIZING DIAGNOSIS AND TREATMENT

SYMPTOMS AND BIOLOGY

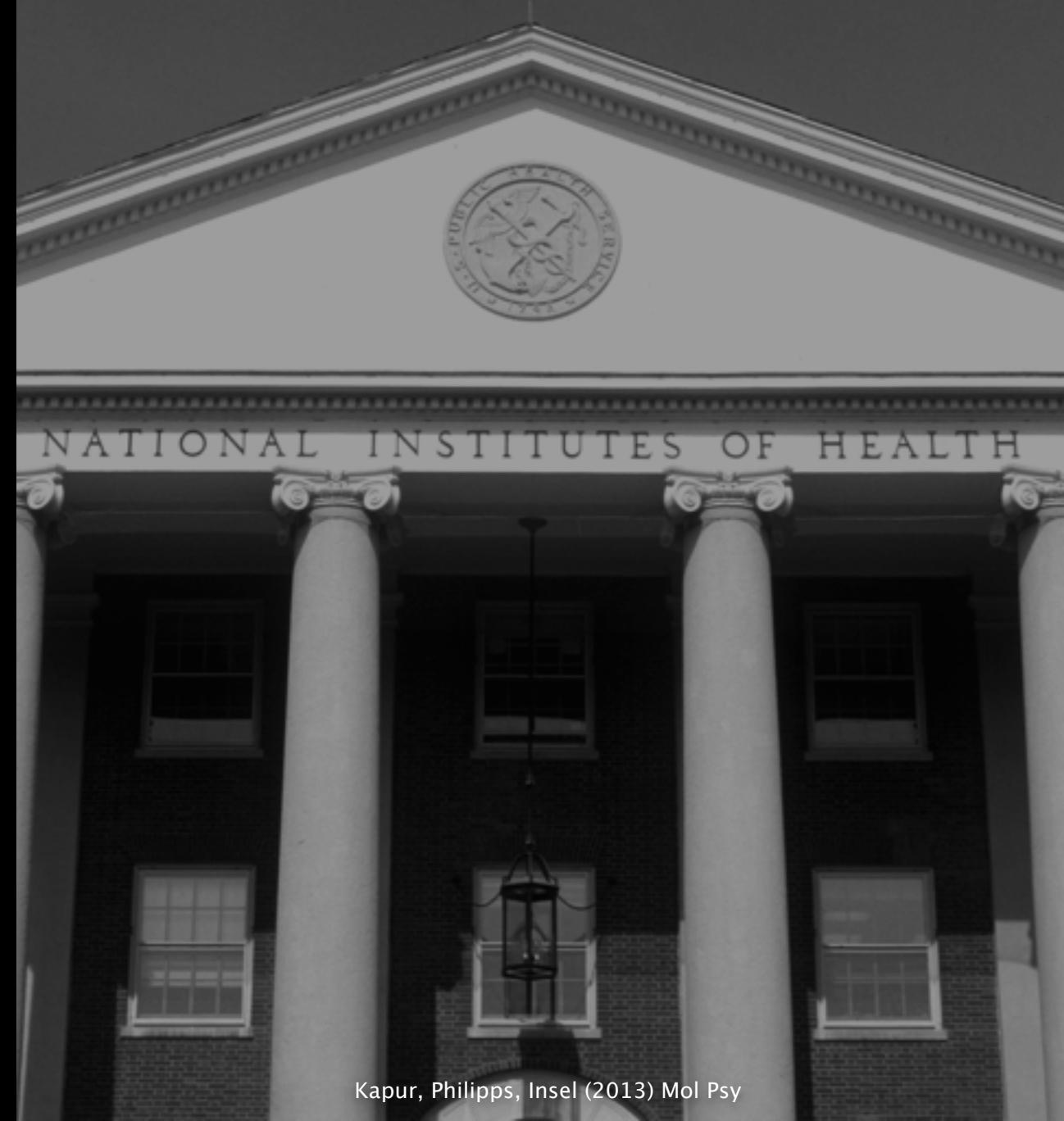
IN ESSENCE, WE WANT TO INCORPORATE
BRAIN-MARKERS INTO PATIENT EVALUATION

SUBTYPING/BIOTYPING

TRANS-DISEASE

TREATMENT BENEFITS:
MATCHING CARE TO BIOLOGY

PROGNOSTIC GAIN



NEUROIMAGING AS A TRANSFORMATIVE TOOL

WIDELY AVAILABLE

NON-INVASIVE

QUANTITATIVE

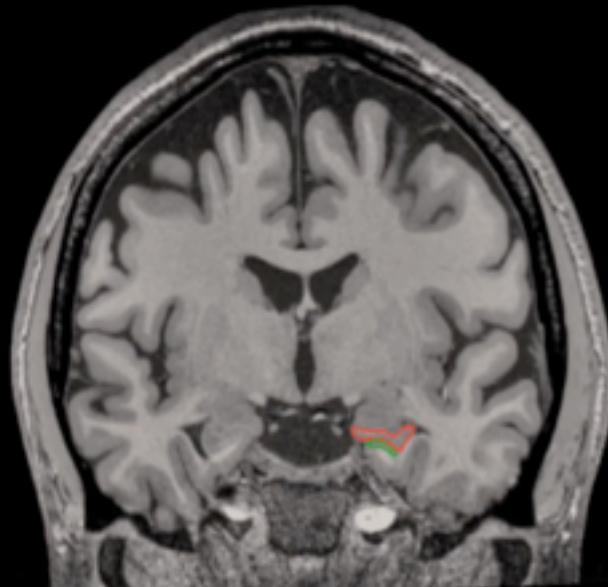
WHOLE BRAIN

VERSATILE

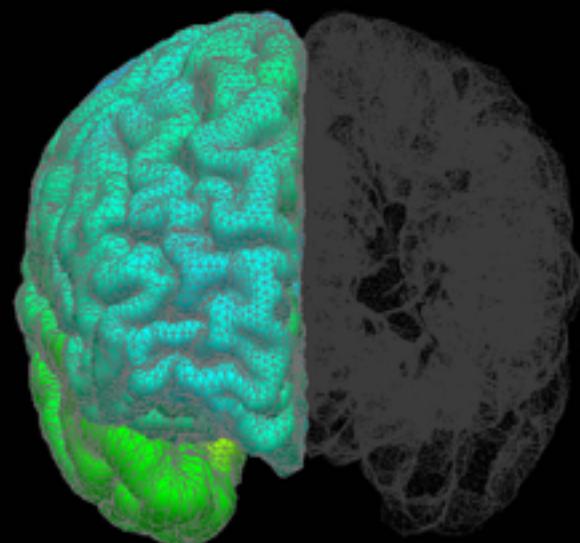


THE POWER OF NEUROIMAGING TO CHARACTERIZE HUMAN BRAIN ORGANIZATION

REGIONAL



WHOLE-BRAIN



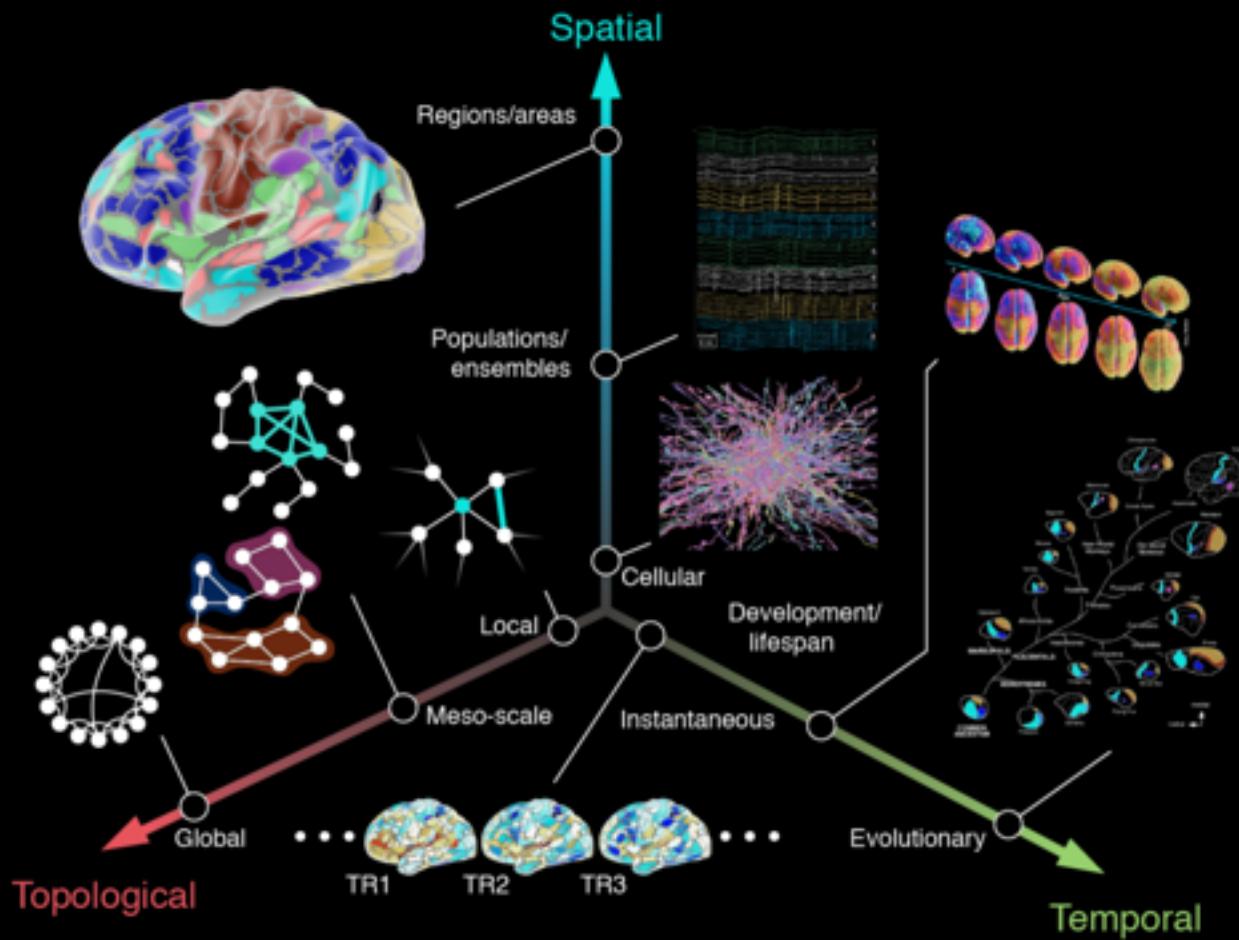
CONNECTOME



Courtesy of Jessie Kulaga-Yoskovitz

Courtesy of Alfred Anwander

THE POWER OF NEUROIMAGING TO CHARACTERIZE HUMAN BRAIN ORGANIZATION



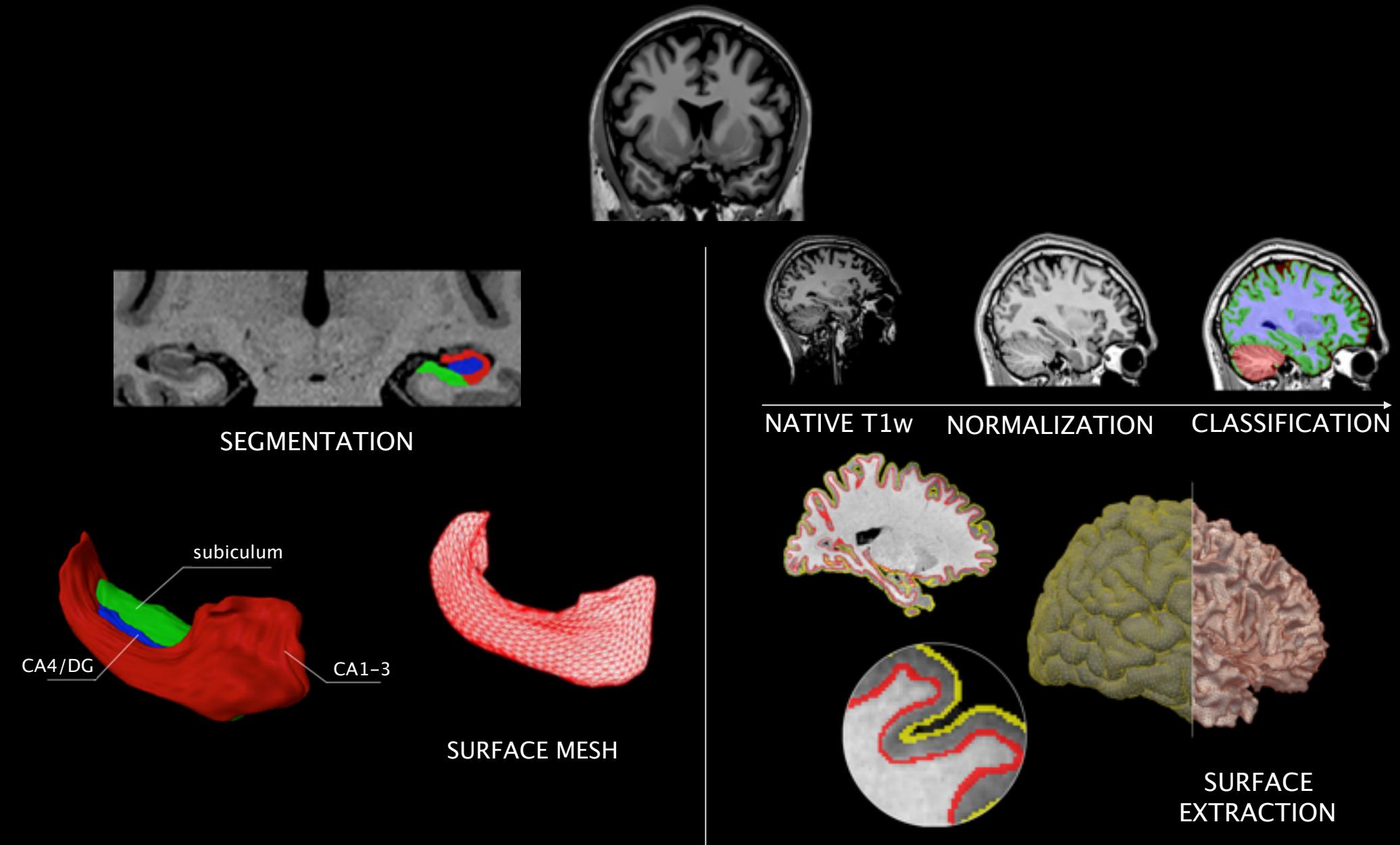
OUTLINE

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

APPLICATION TO EPILEPSY:
INTEGRATING HIGH-DEF MRI WITH LARGE-SCALE NETWORKS
TO INFER HISTOPATHOLOGY, SURGICAL OUTCOMES, AND DISEASE MECHANISMS

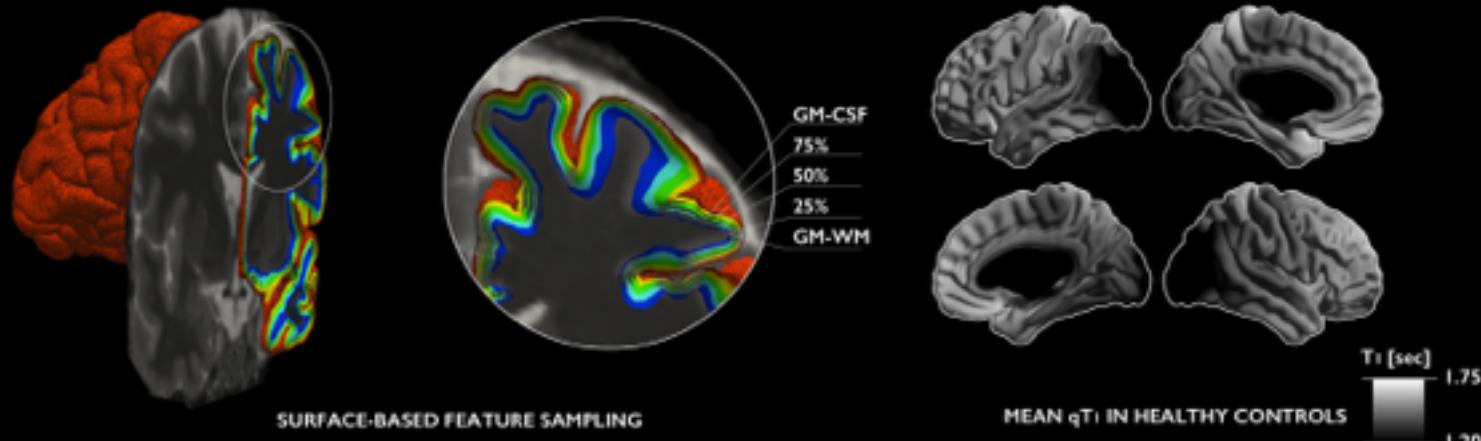
STUDIES IN AUTISM:
NEUROIMAGING-DERIVED ASD SUBTYPING AND
THE INTERPLAY BETWEEN CORTICAL MORPHOLOGY AND CONNECTOMICS

MODELLING LOCAL STRUCTURE

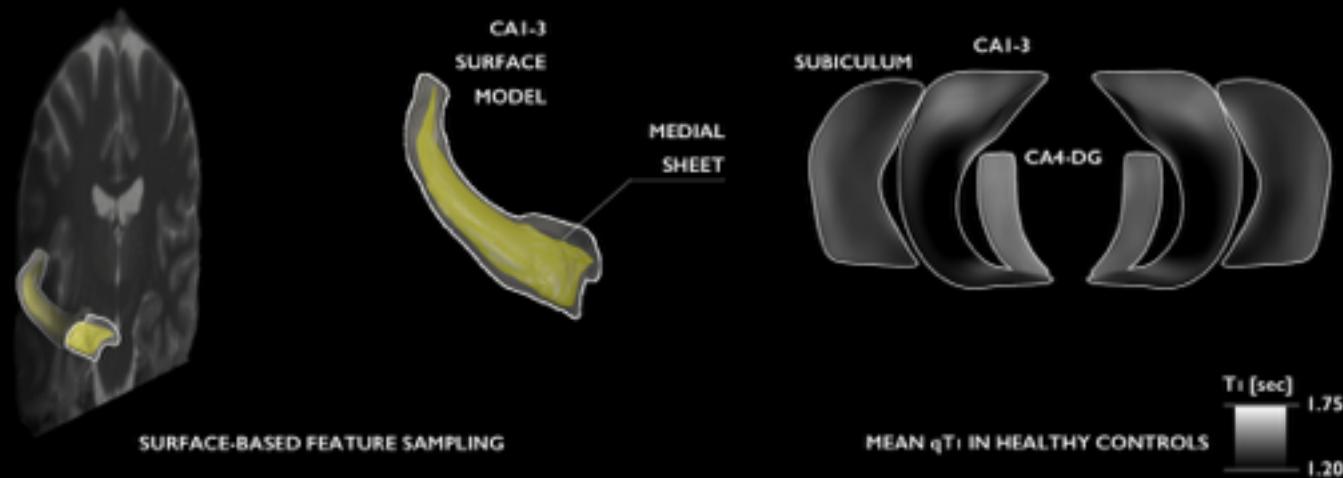


MODELLING LOCAL STRUCTURE

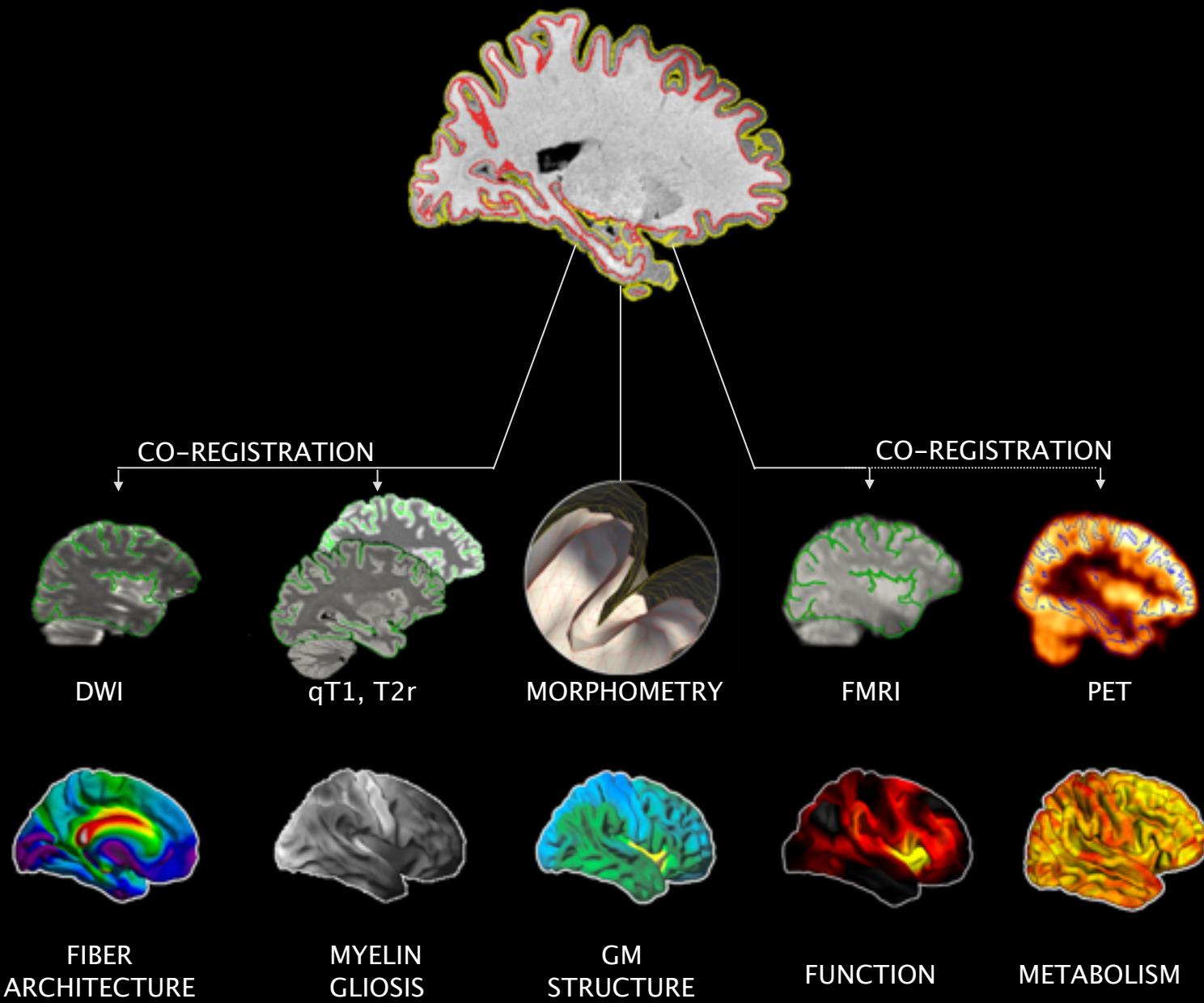
A NEOCORTICAL qT_1 MAPPING



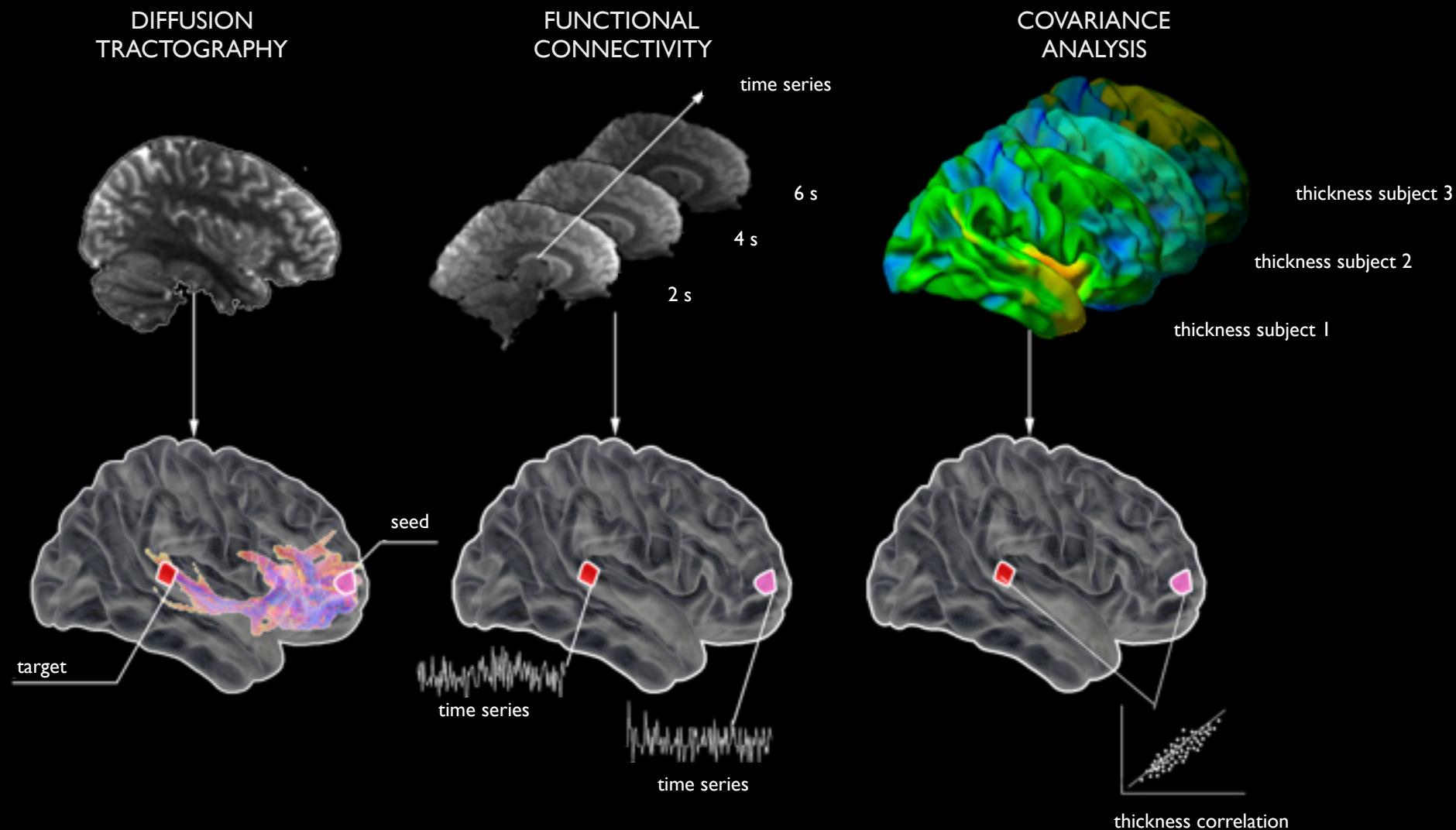
B HIPPOCAMPAL qT_1 MAPPING



MULTIMARKER INTEGRATION



INTER-REGIONAL CONNECTIVITY ANALYSIS

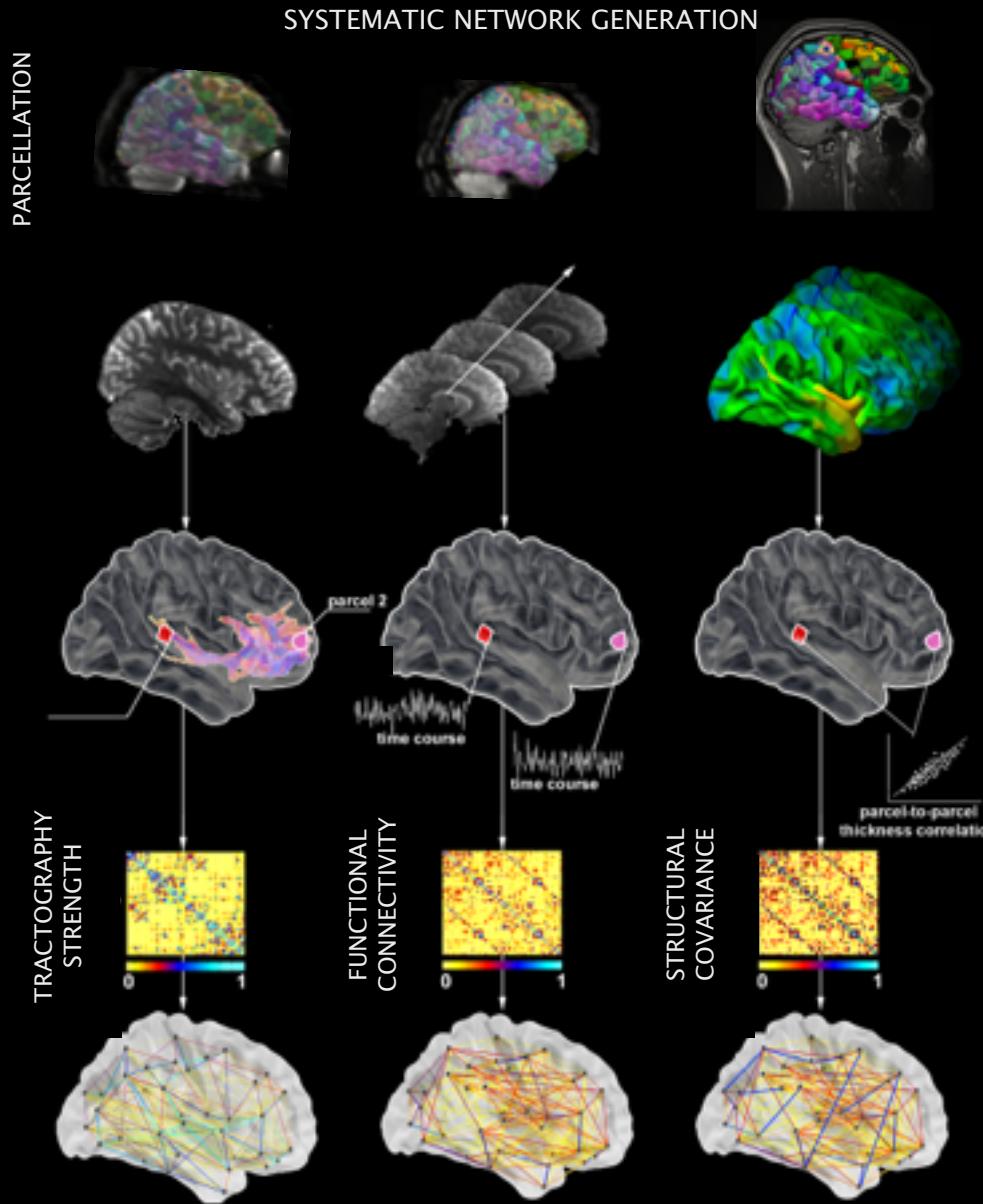


Mori et al. (1999) Ann Neu
Behrens et al. (2007) NIMG

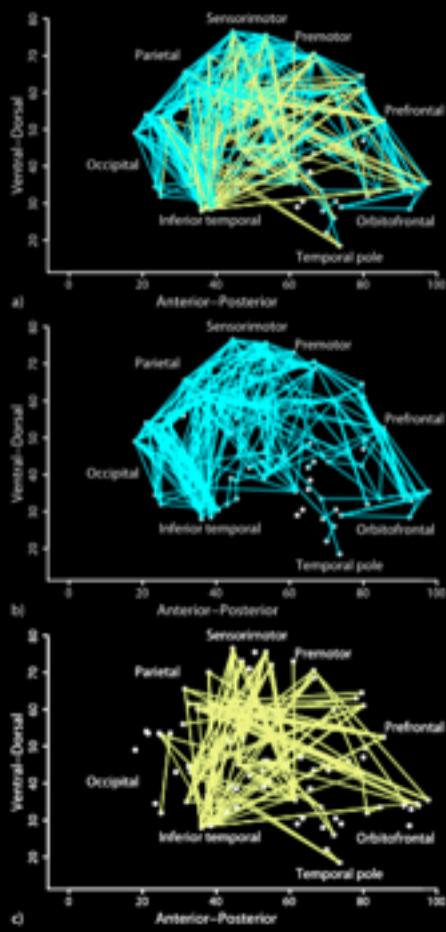
Biswal (1995) MRM
Friston (1994) HBM
Smith (2012) NIMG

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

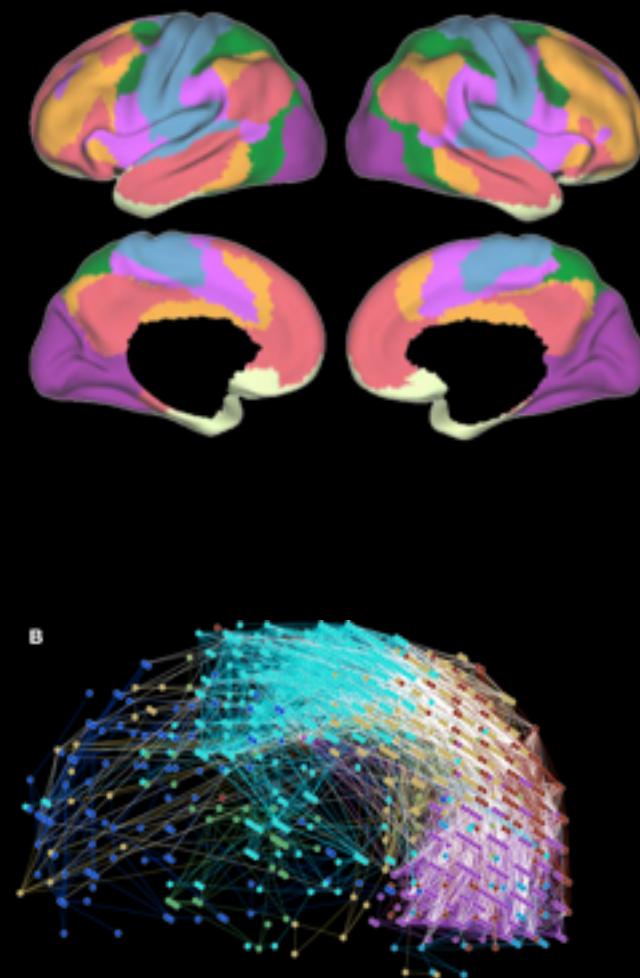
CONNECTOME SCALE



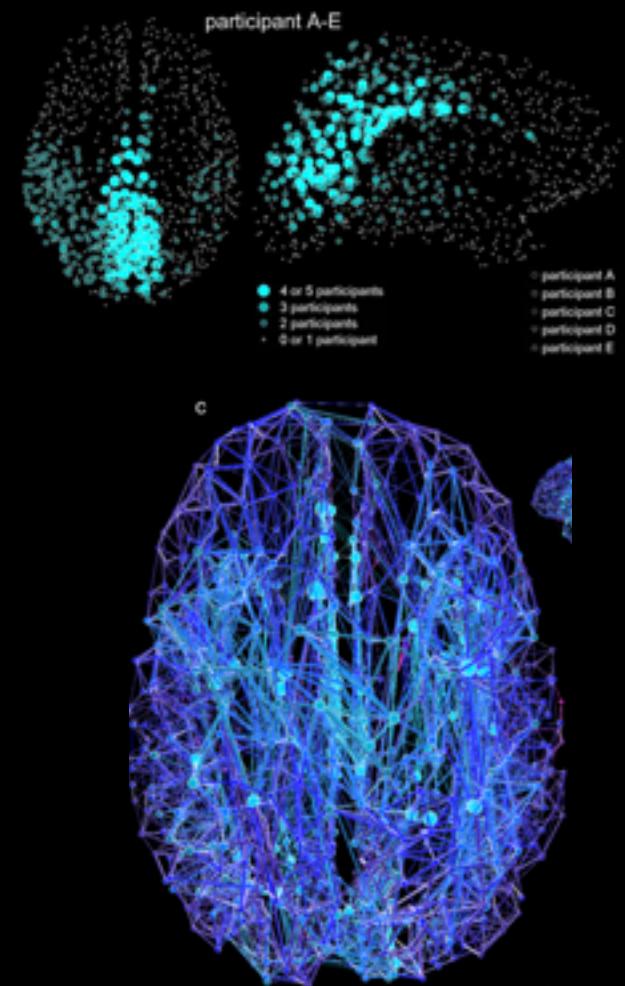
CONNECTOME SCALE



Archard 2006 JN



Yeo 2011 J Neurophysiol
Meunier (2006) Fron Neuroinf



Hagman 2008 PloS Comp Biol
Van den Heuvel 2013 JN

EPILEPSY

CHRONIC SEIZURES

0.5–1.5% OF POPULATION

HETEROGENOUS

30% OF PATIENTS ARE
DRUG-RESISTANT

MULTIDISCIPLINARY
ASSESSMENT



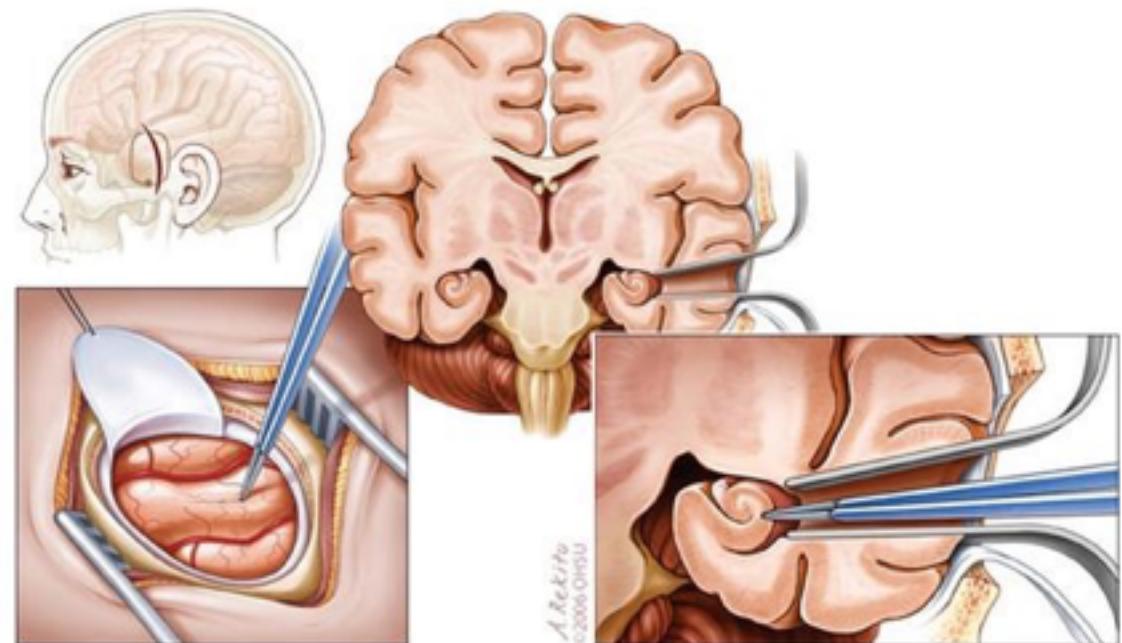
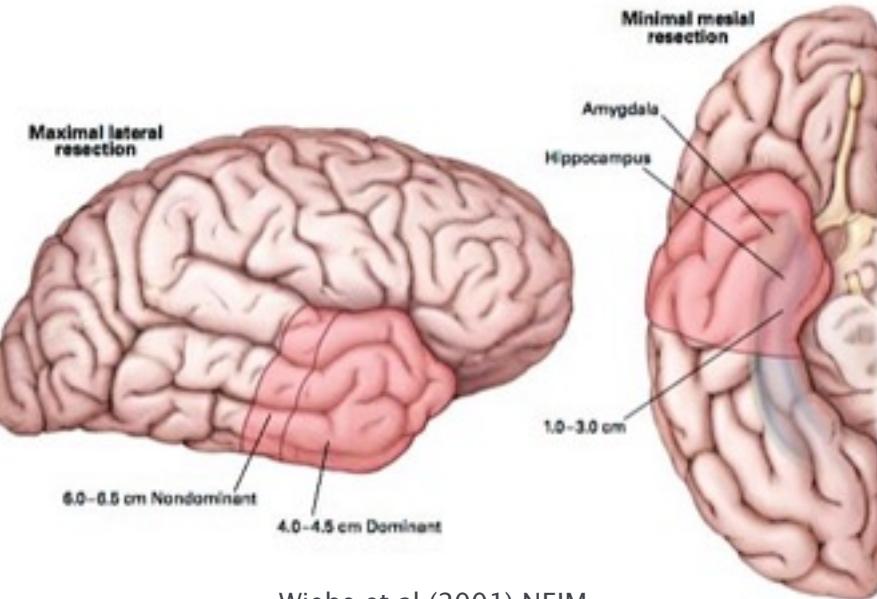
TEMPORAL LOBE EPILEPSY

ONE OF THE MOST COMMON
DRUG-RESISTANT
EPILEPSIES IN ADULTS

SEIZURES ARISING FROM TL

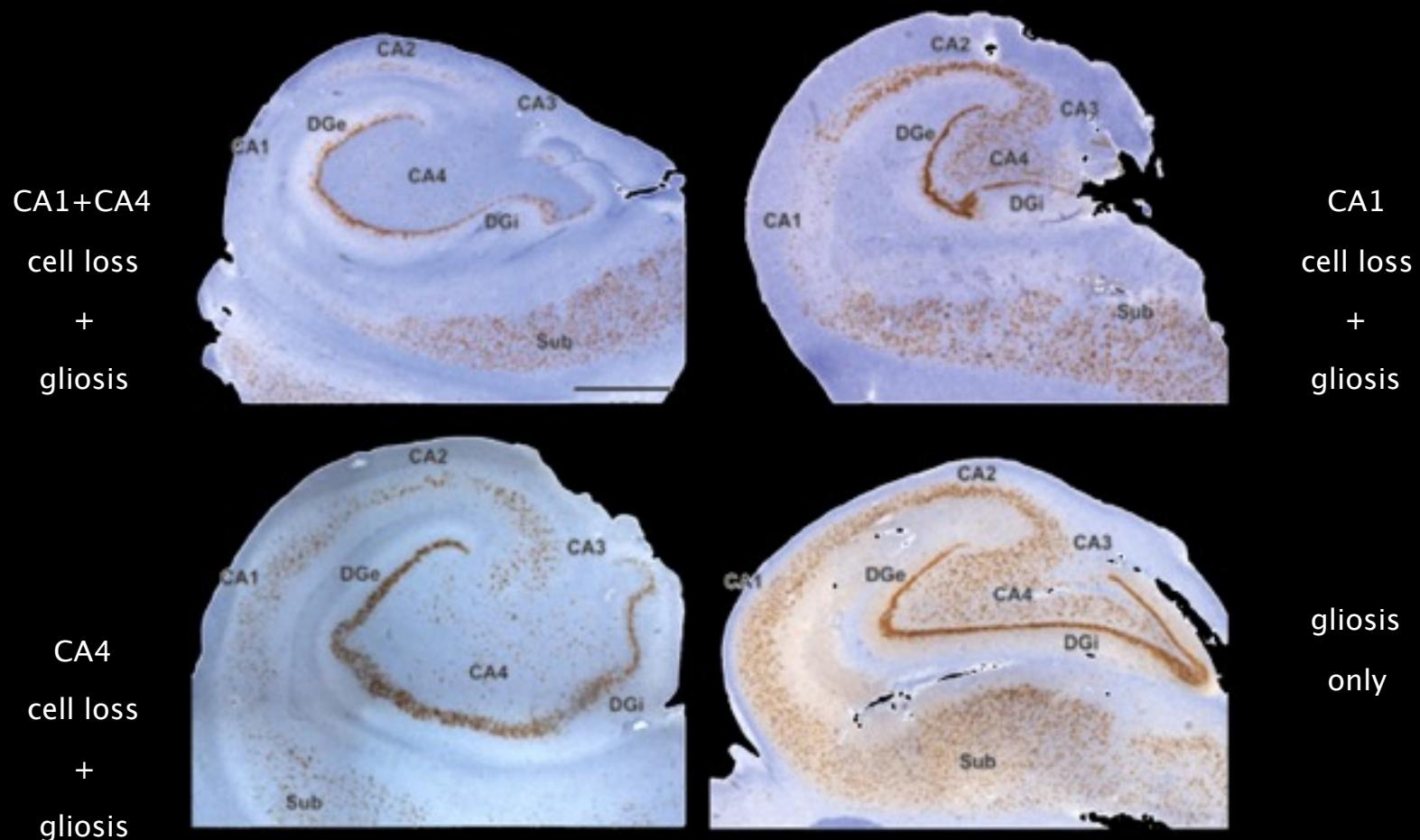
SURGERY MOST EFFECTIVE
TREATMENT

ASSOCIATED WITH
HIPPOCAMPAL SCLEROSIS (HS)

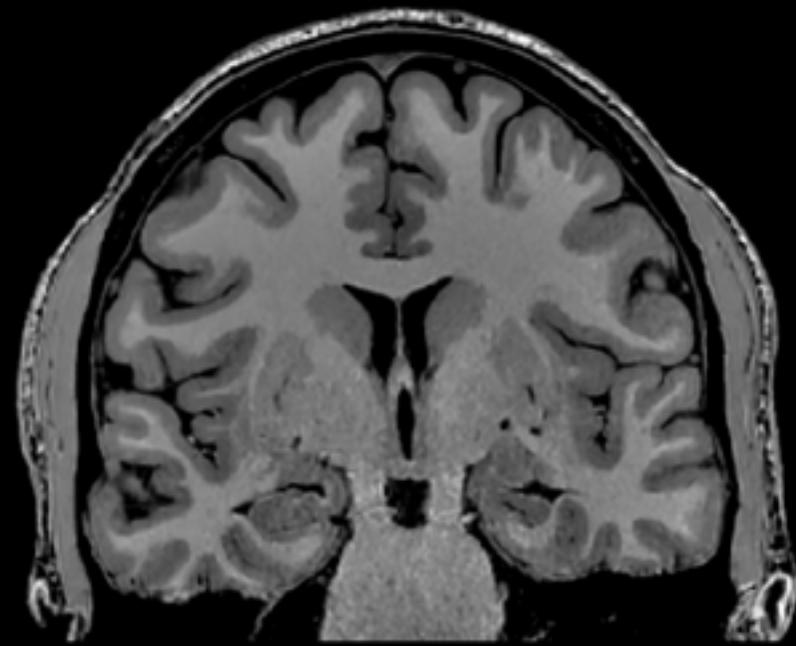


TEMPORAL LOBE EPILEPSY

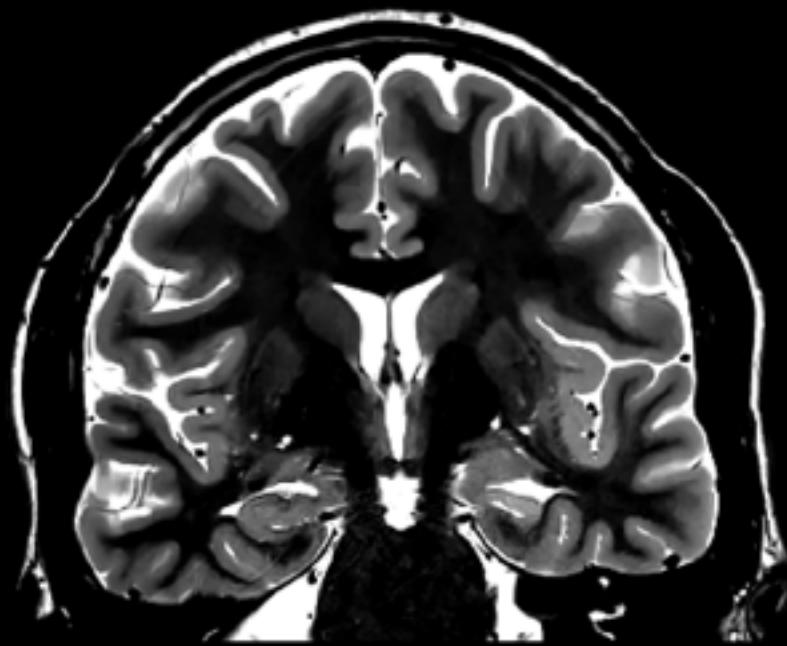
HS IS THE TLE HALLMARK BUT NOT A SINGLE ENTITY



THE CONTRIBUTIONS OF NEUROIMAGING TO TLE EVALUATION AND DIAGNOSIS OF HS



T1-weighted

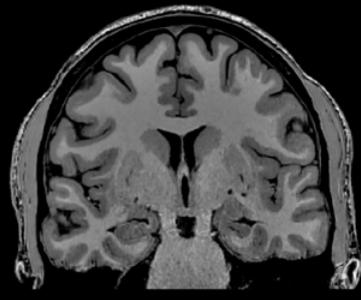


T2-weighted

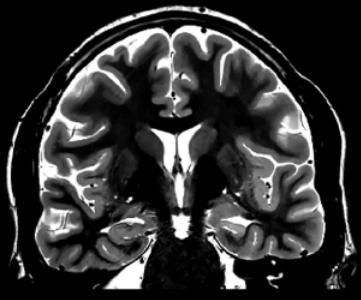
CAN WE DESCRIBE THE PATHOLOGICAL SPECTRUM OF TLE IN-VIVO?
DO STRUCTURAL CHANGES RELATE TO FUNCTIONAL NETWORK
ALTERATIONS?

STUDY DESIGN

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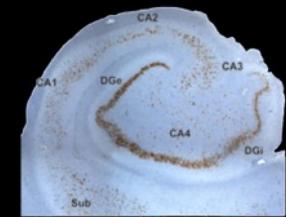
T1-weighted



T2-weighted

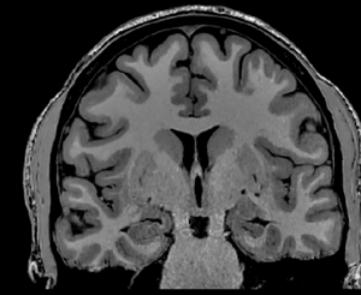


SURGERY

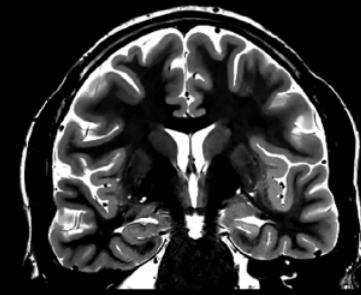


HS

19



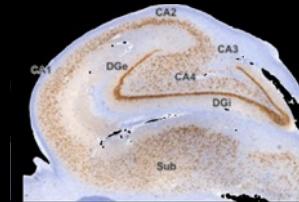
T1-weighted



T2-weighted

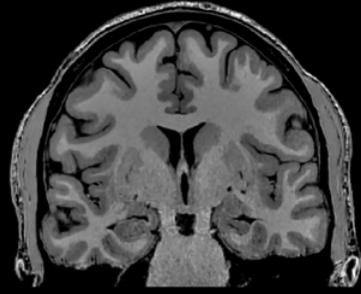


SURGERY

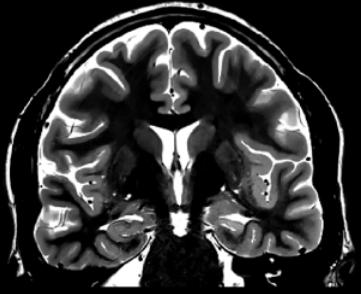


GLIOSIS

25



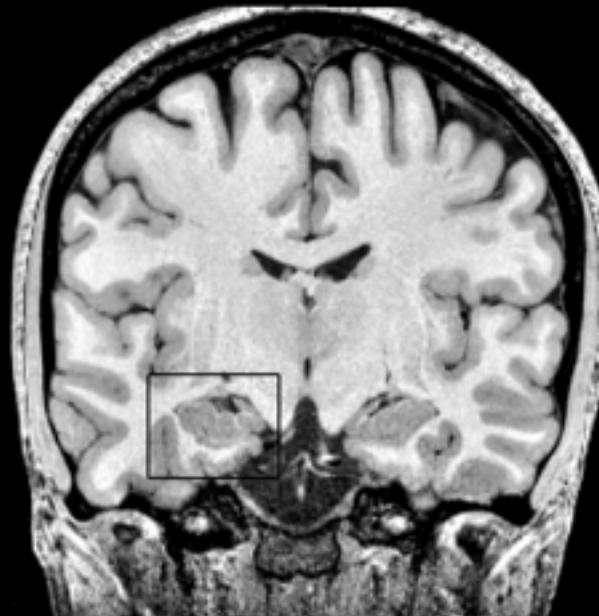
T1-weighted



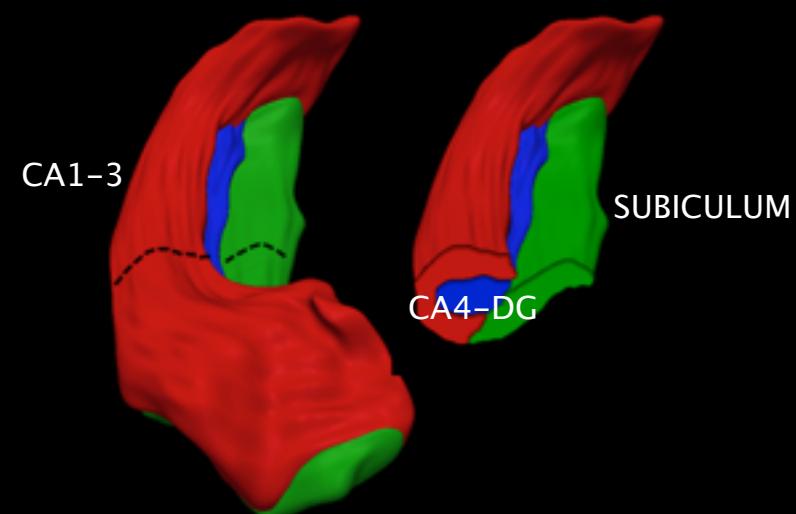
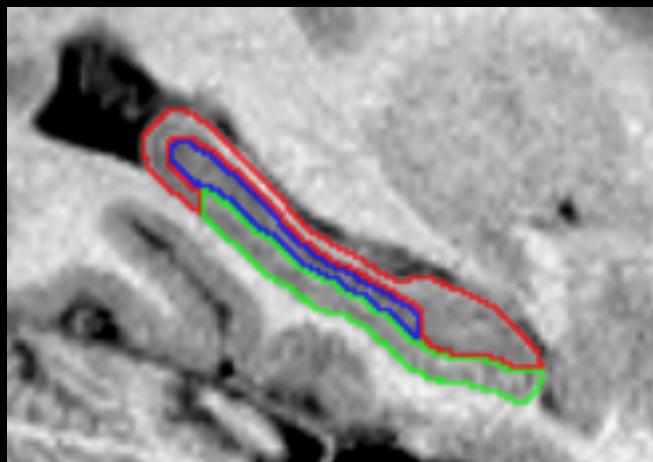
T2-weighted

3T MRI DATA

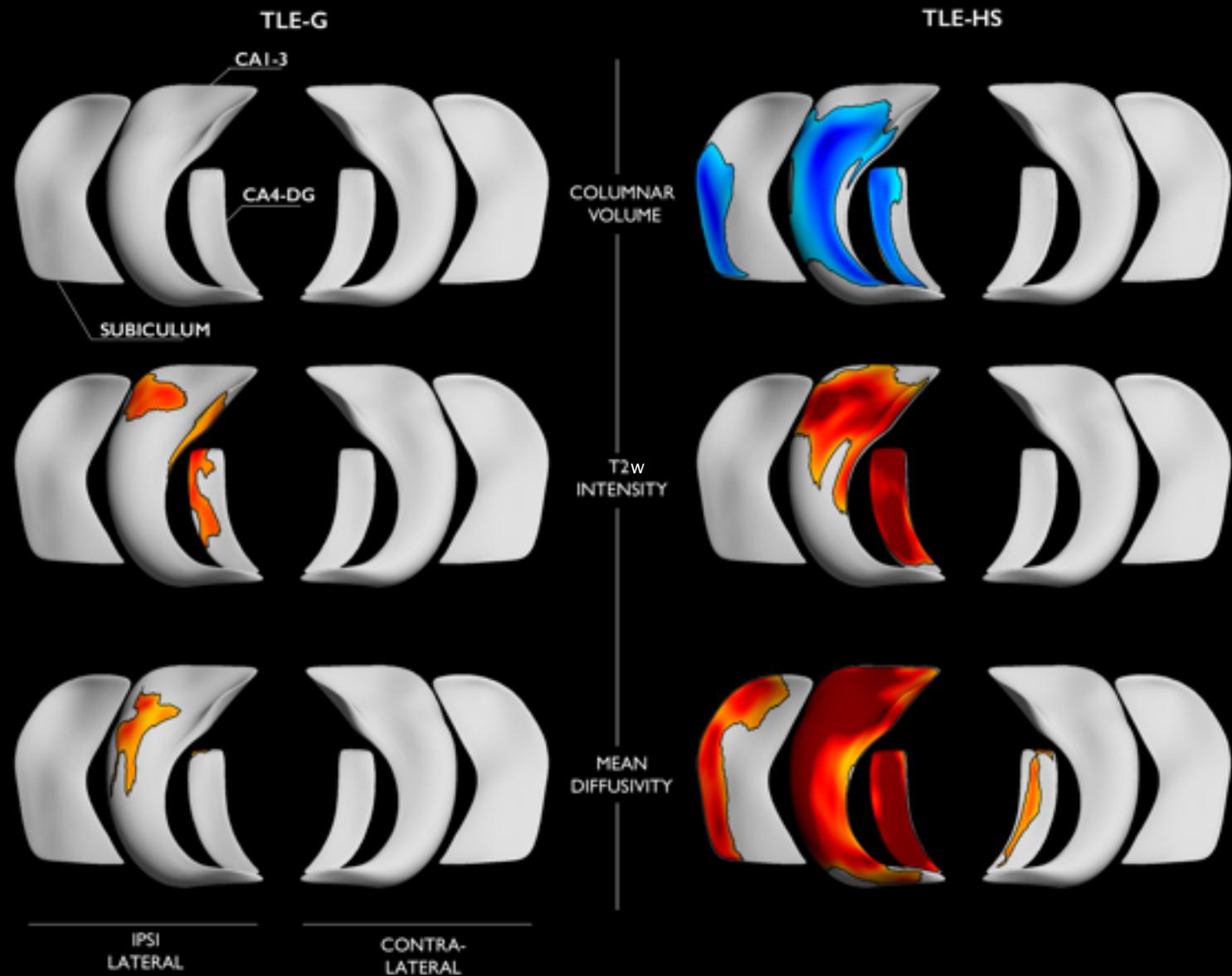
CONTROLS



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

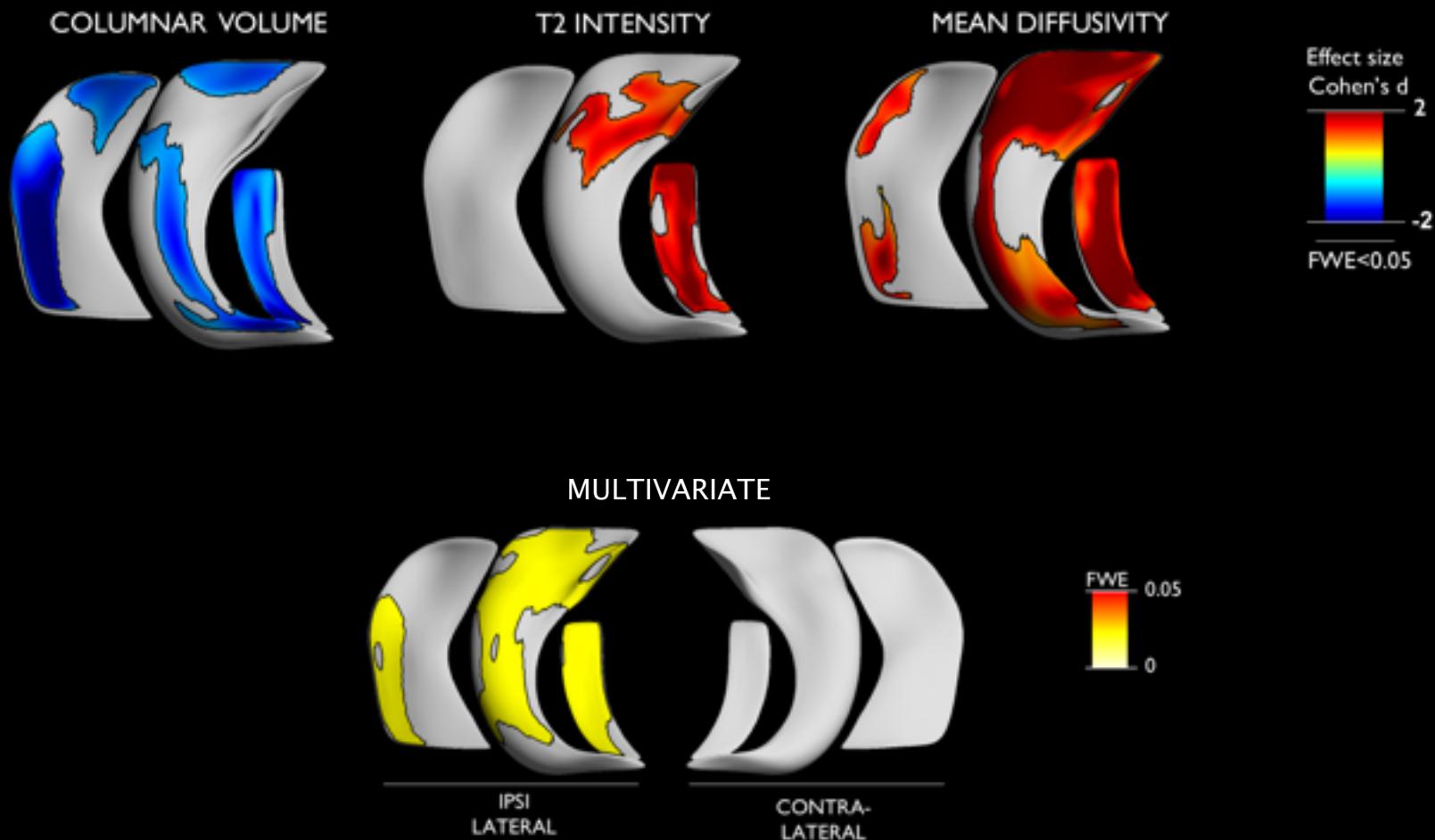


FEATURE-SPECIFIC COMPARISON TO CONTROLS



DIRECT CONTRASTS

B DIRECT CONTRAST: TLE-HS vs TLE-G

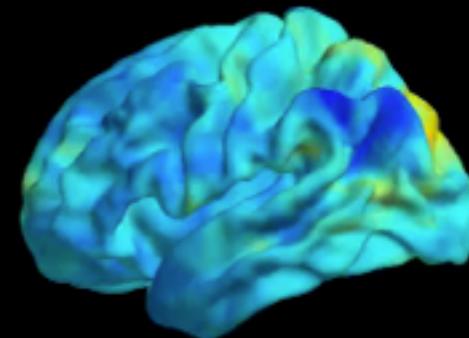


FUNCTION

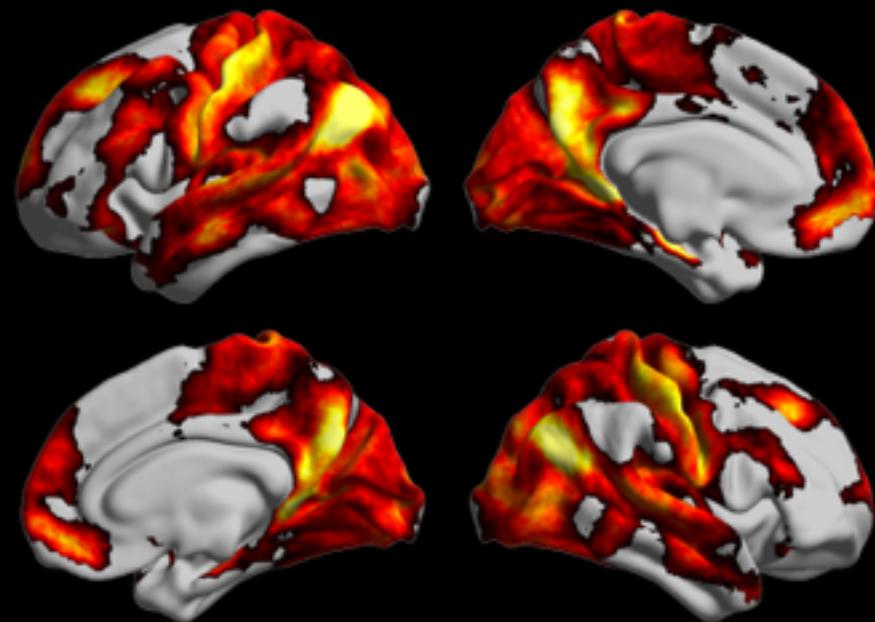
rs-FMRI ANALYSIS OF
INTRINSIC FUNCTIONAL NETWORKS

HIPPOCAMPUS HIGHLY INTEGRATED
WITH DMN

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



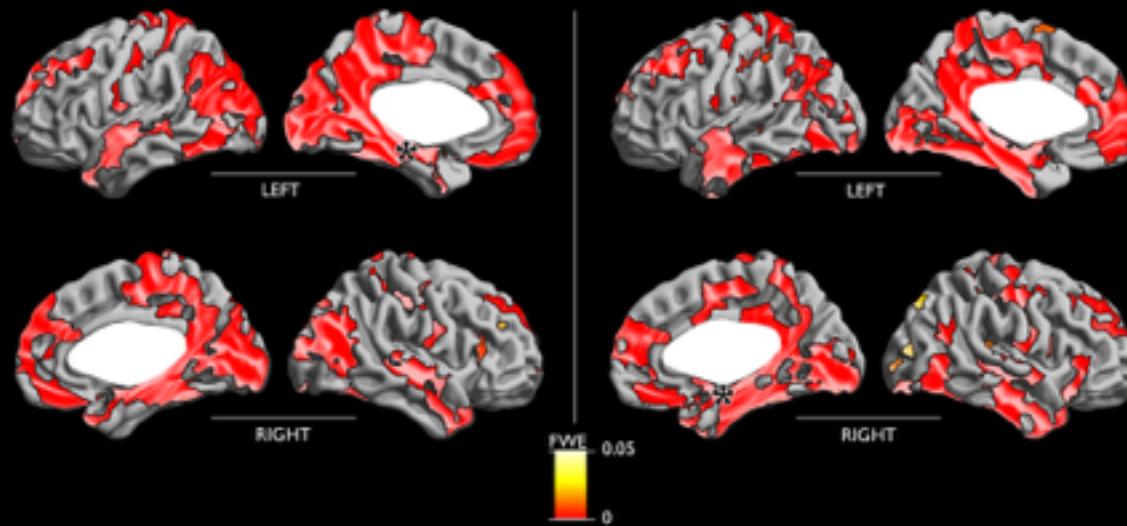
Brain at rest



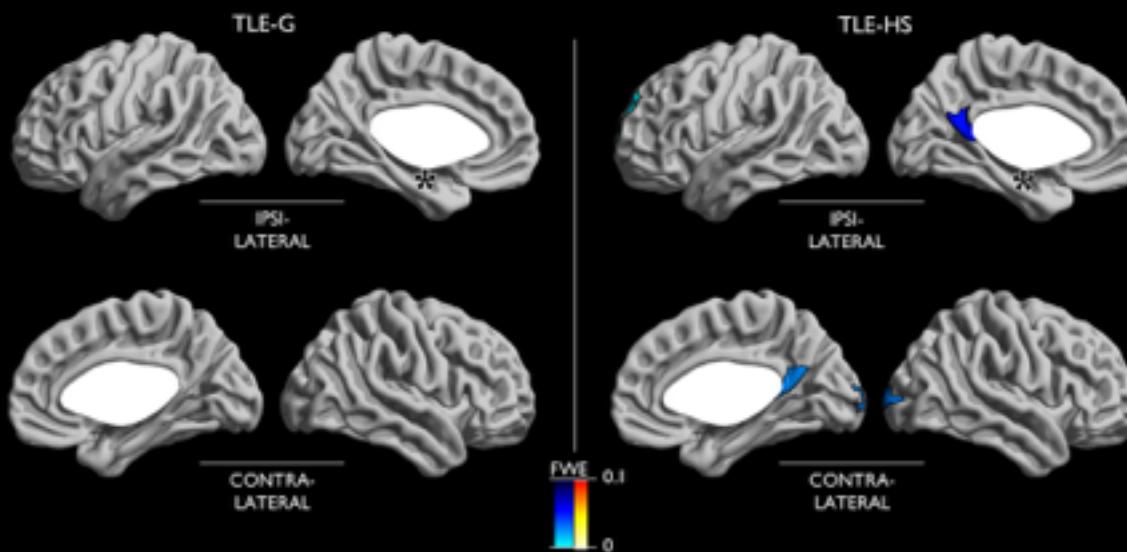
HCP hippocampal connectivity

FUNCTIONAL ANOMALIES IN TLE

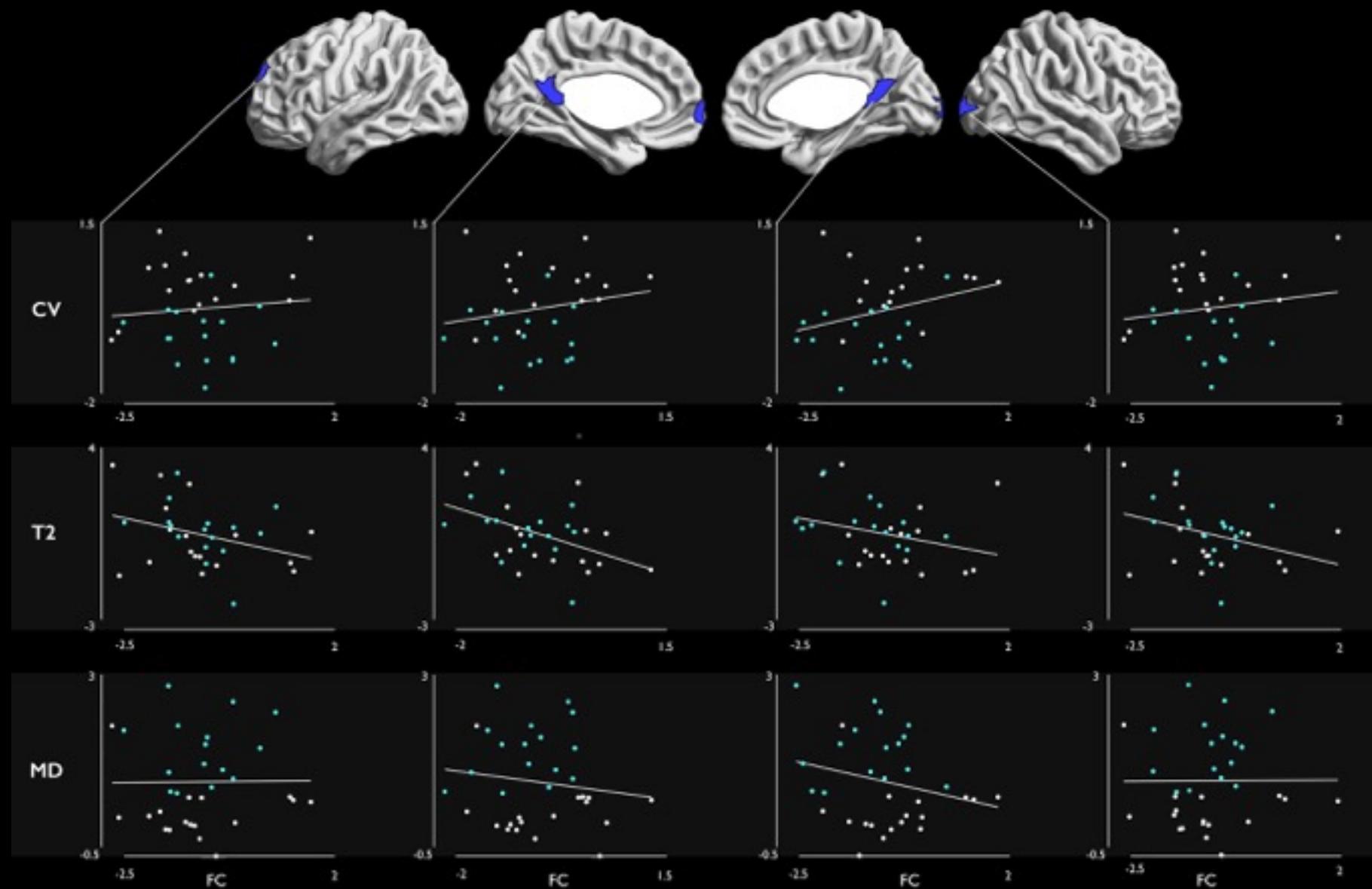
A CONNECTIVITY IN CONTROLS



B CONNECTIVITY ALTERATIONS IN TLE

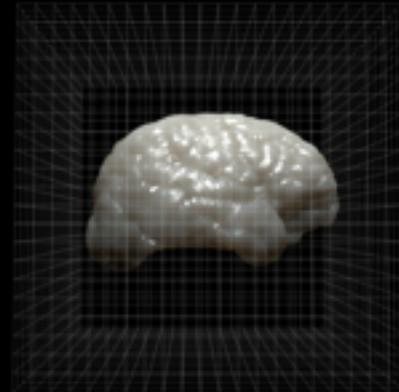


STRUCTURE-FUNCTION RELATIONSHIPS IN TLE

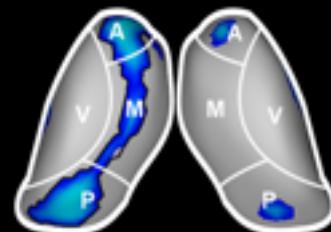


DO ANOMALIES EXTEND BEYOND THE MESIOTEMPORAL REGIONS?

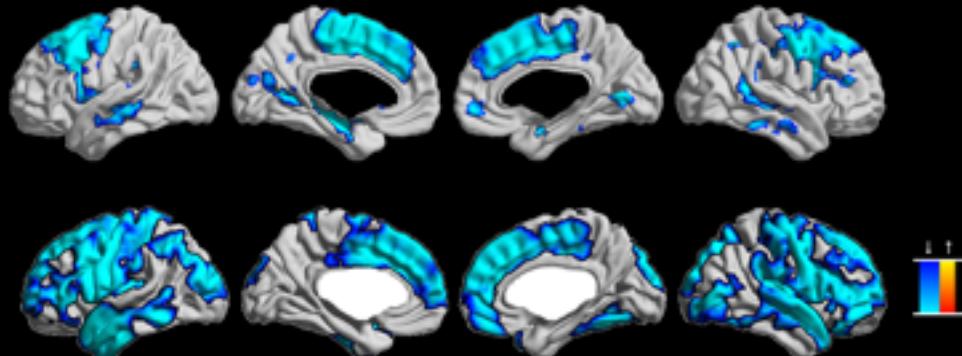
WHOLE-BRAIN GREY MATTER



Keller 2002 JNNP, Bonilha 2004/06 NIMG, Bernasconi 2004 NIMG

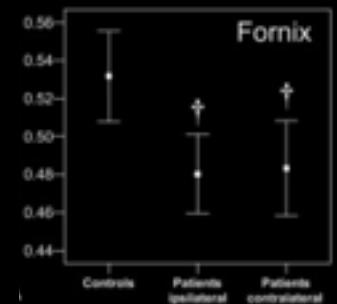
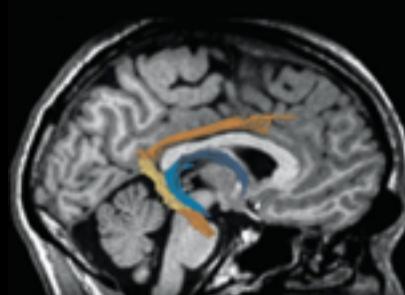


Neurology 2012

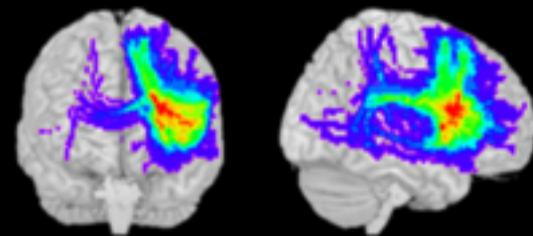


Lin 2007 CerCor, McDonald 2008 Epilepsy, Bernhardt 2008 NIMG

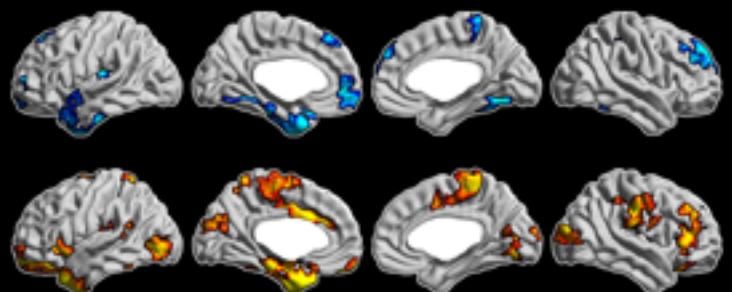
WHOLE-BRAIN WHITE MATTER



Concha 2005 Ann Neu



Powell 2006 NIMG

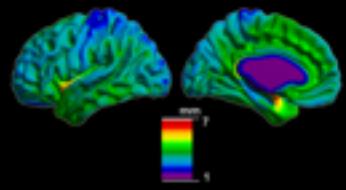


Liu 2016 Brain

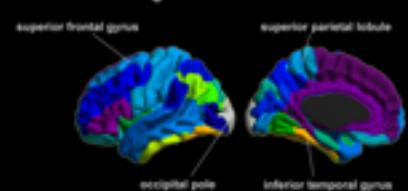
MACROLEVEL STRUCTURAL NETWORK GENERATION

NEOCORTEX

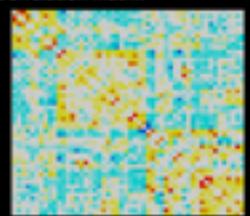
A. Cortical thickness measurements



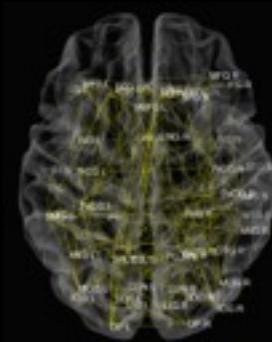
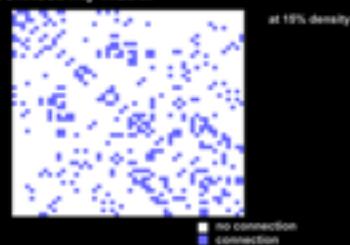
B. Anatomical segmentation



C. Correlation matrix

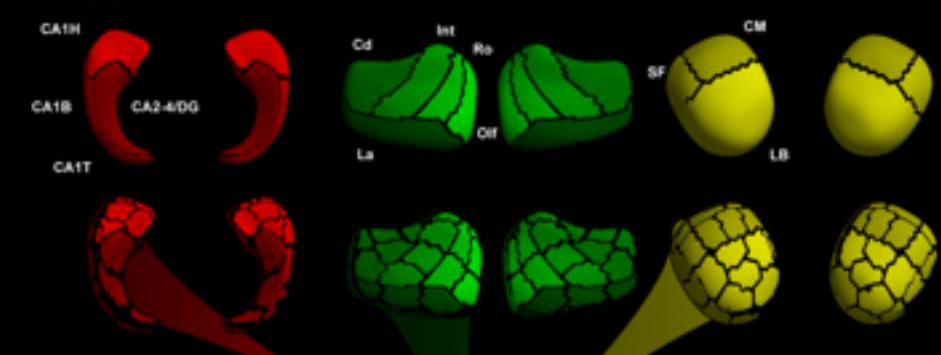


D. Connectivity matrix

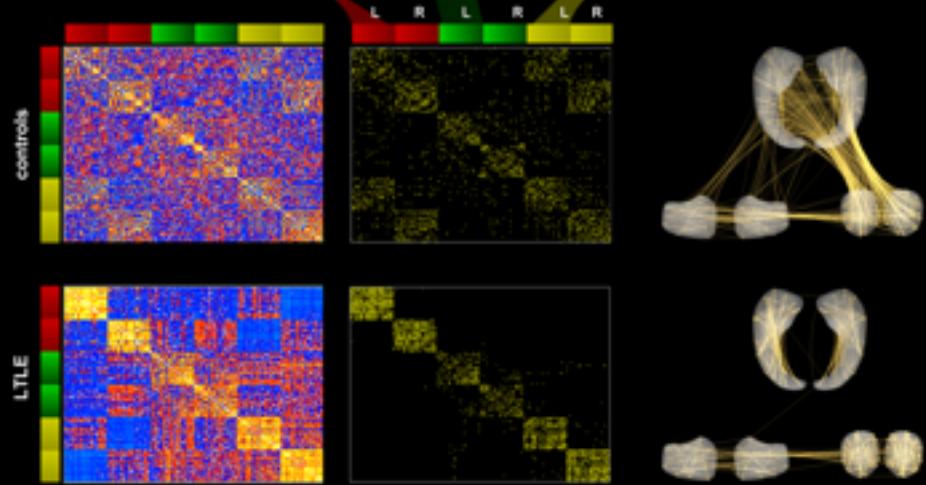


MESIOTEMPORAL LOBE

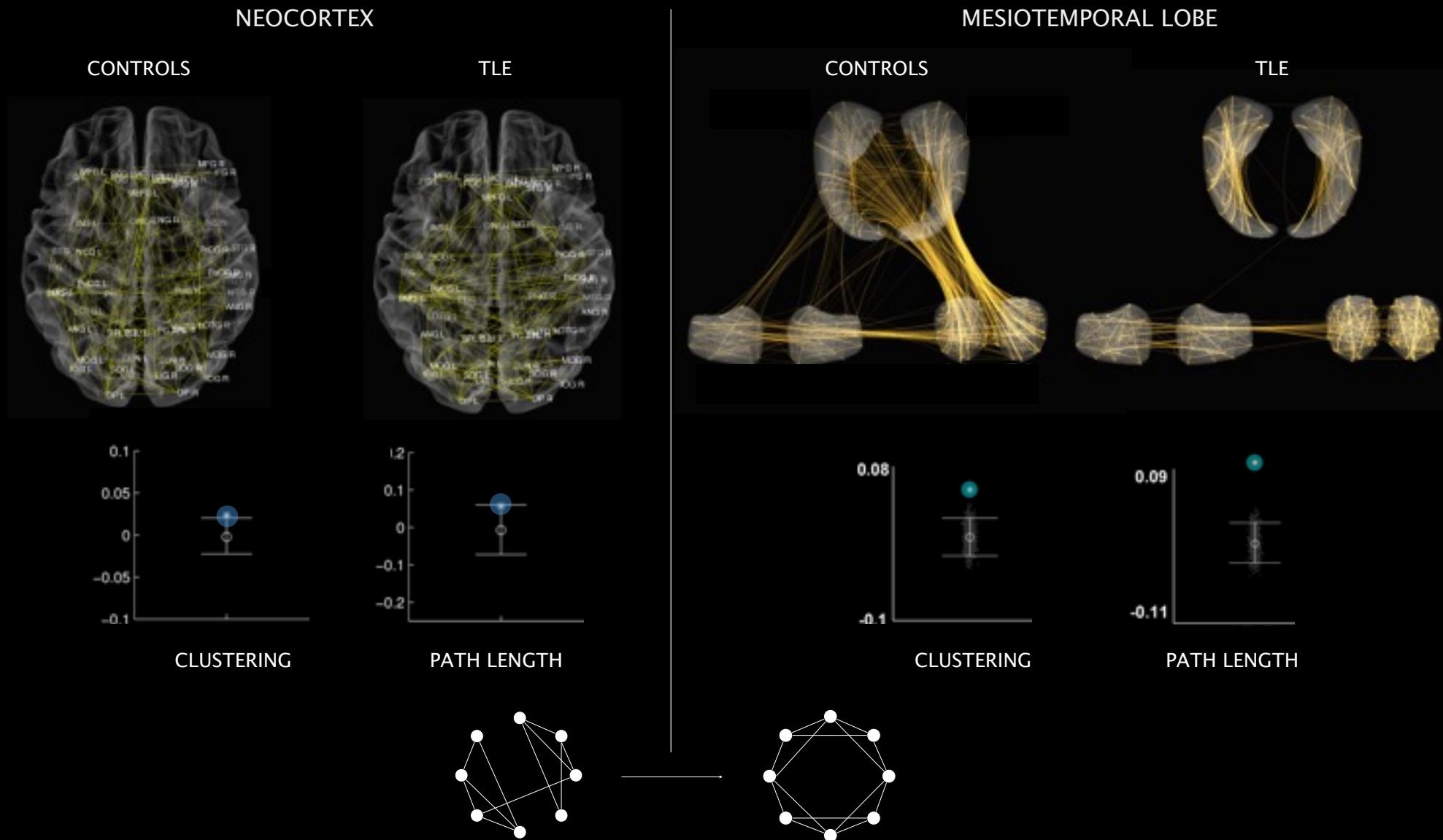
A. Parcels



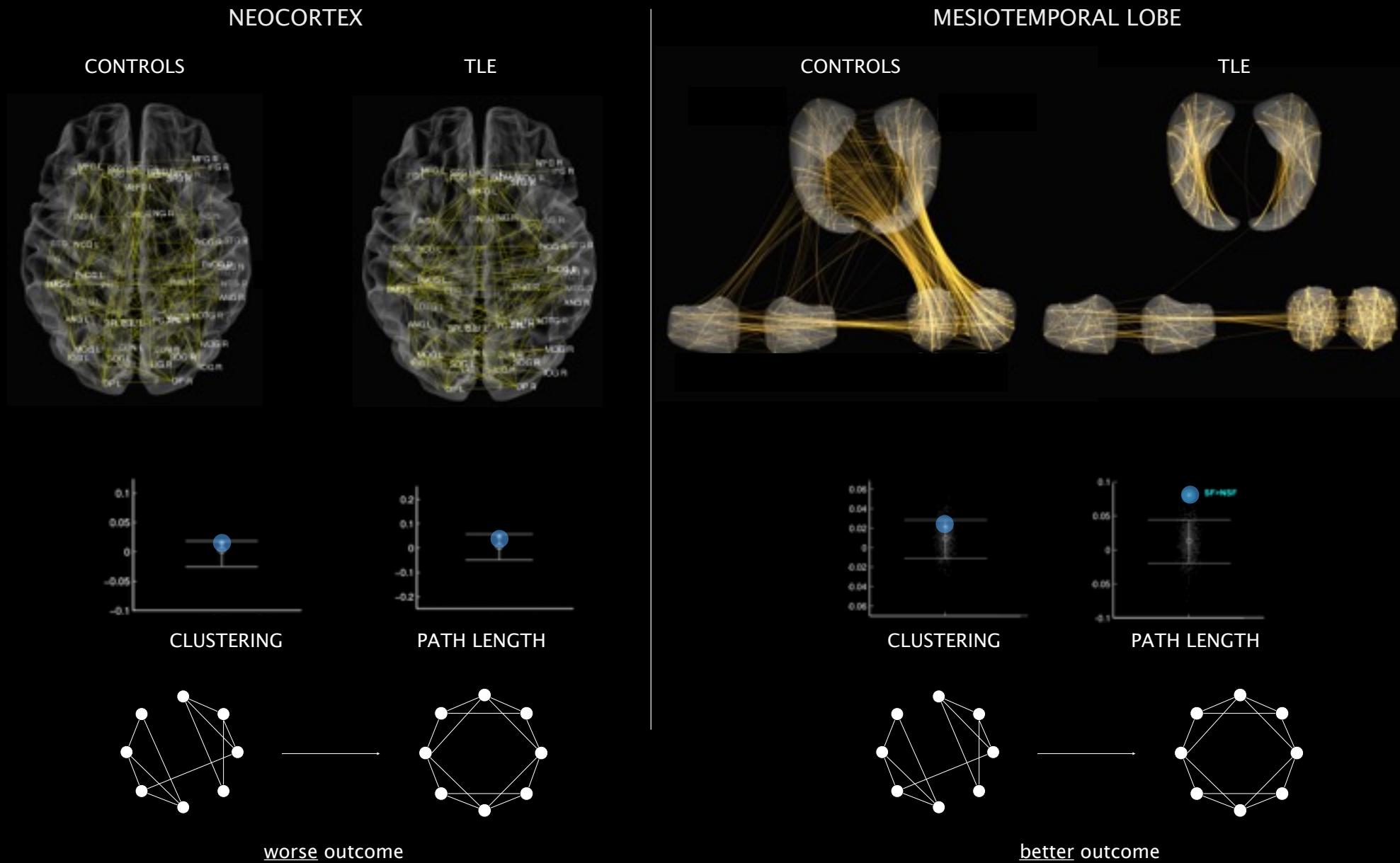
B. Structural covariance network construction



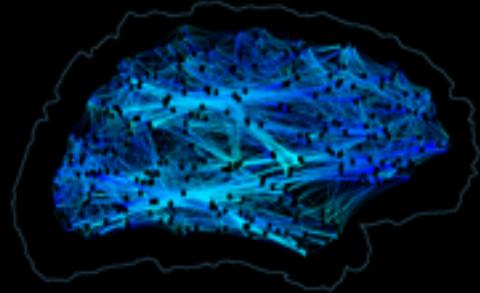
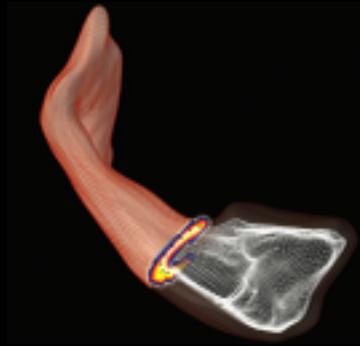
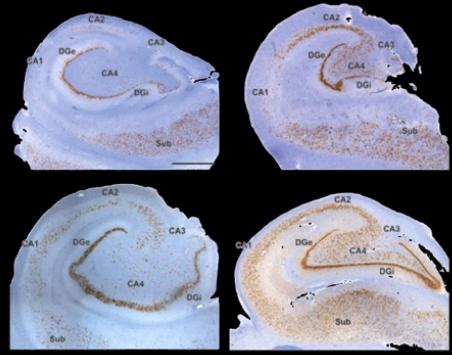
MACROLEVEL STRUCTURAL NETWORK ALTERATIONS



RELATIONSHIP TO OUTCOME

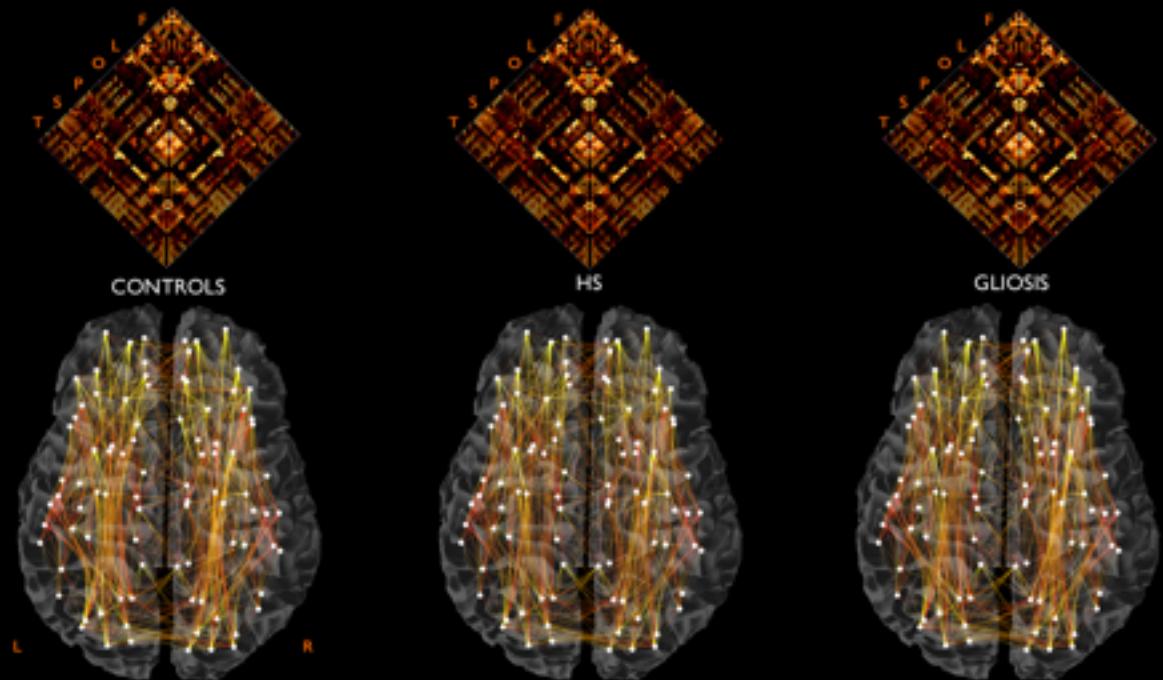


IS THERE A RELATION BETWEEN
HS PATHOLOGY AND MACROSCALE NETWORK ANOMALIES?

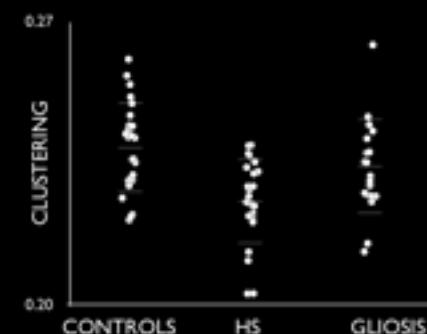
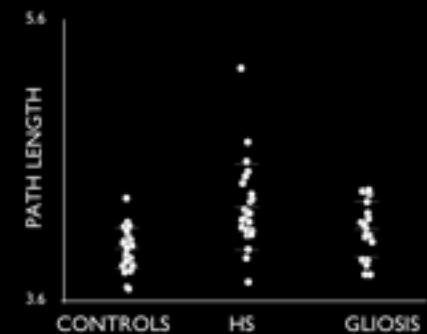


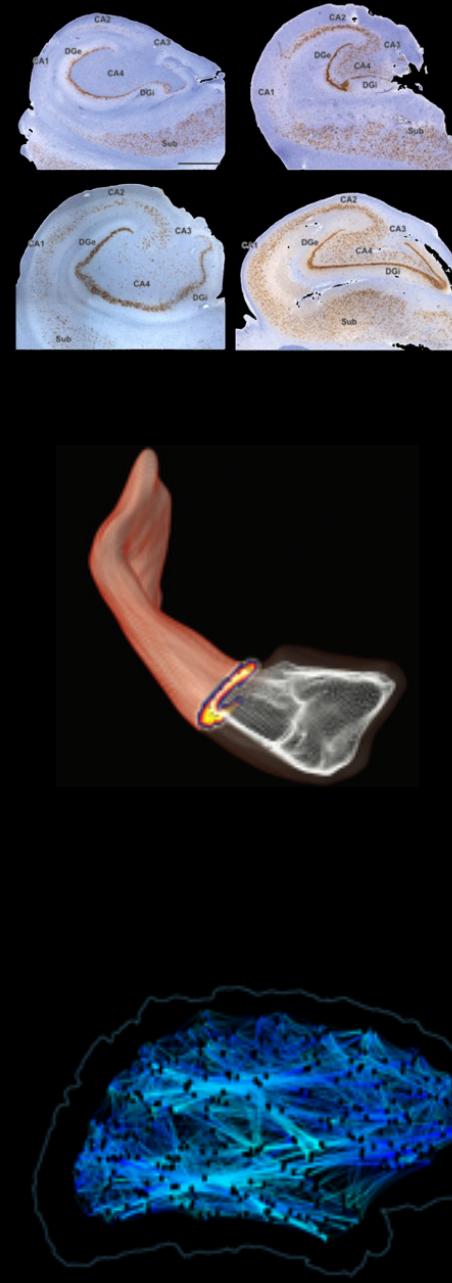
LINKING MACRO/MICROLEVEL DISRUPTIONS

A STRUCTURAL CONNECTOMES



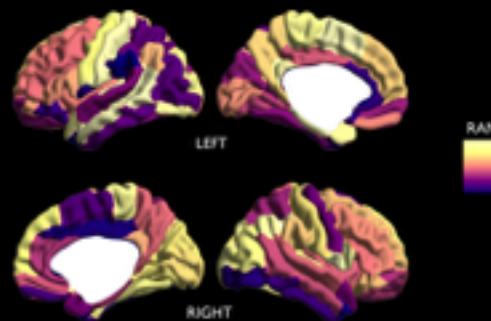
B TOPOLOGICAL PARAMETER ANALYSIS



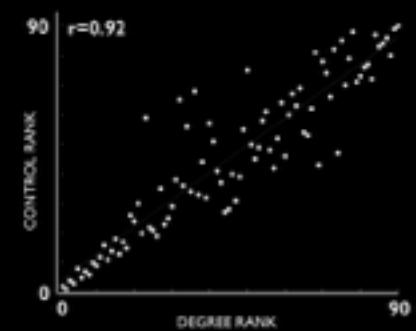


LINKING MACRO/MICROLEVEL DISRUPTIONS

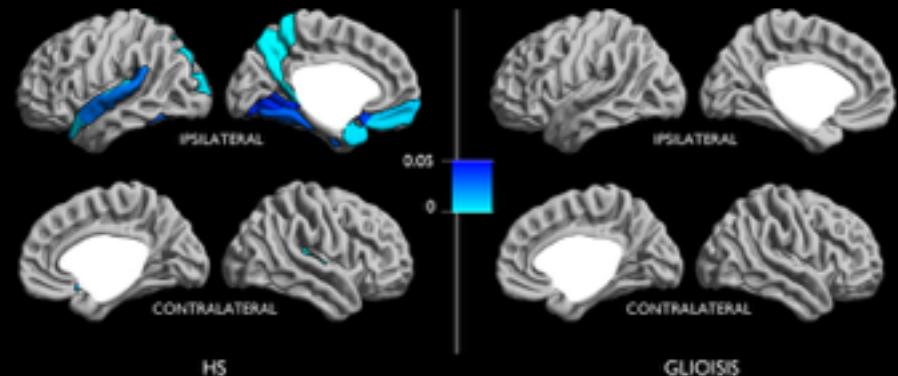
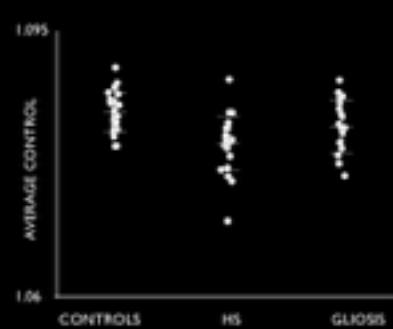
A NETWORK CONTROLLABILITY

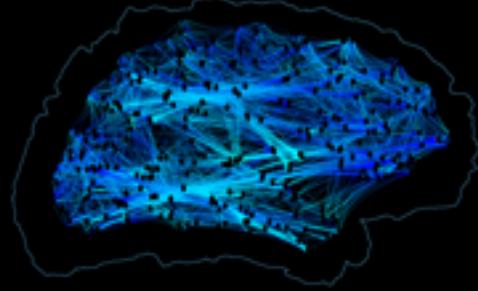
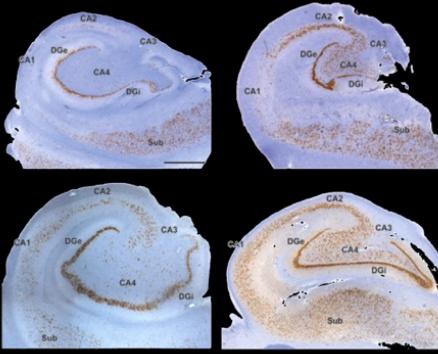


B RELATION TO CENTRALITY



C CONTROLLABILITY ALTERATIONS IN TLE



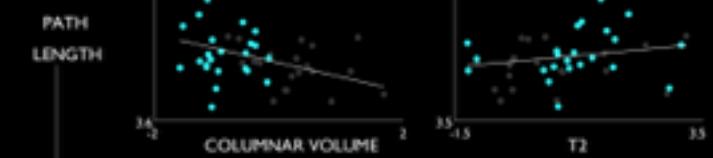
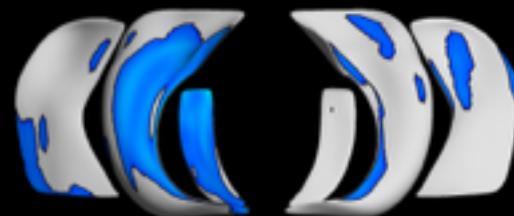
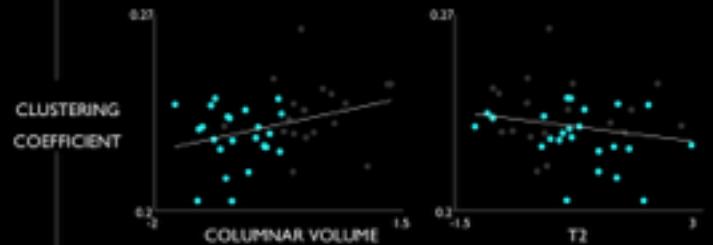


LINKING MACRO/MICROLEVEL DISRUPTIONS

MULTIVARIATE SURFACE-WIDE



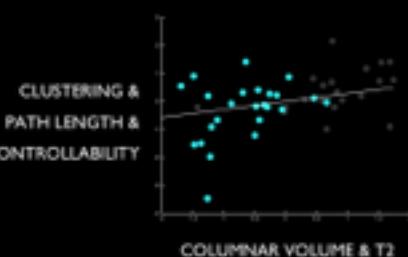
UNIVARIATE POSTHOC

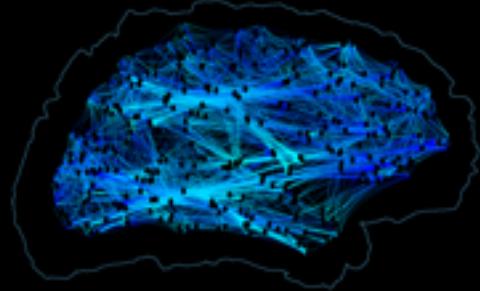
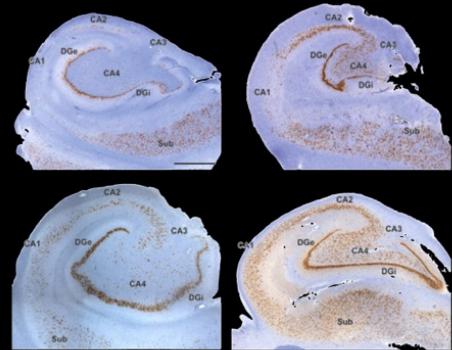


FORKBS
CLUSTERING &
PATH LENGTH &
CONTROLLABILITY

INTERSECTION

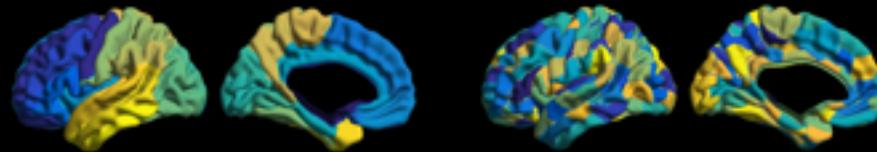
MULTIVARIATE POSTHOC



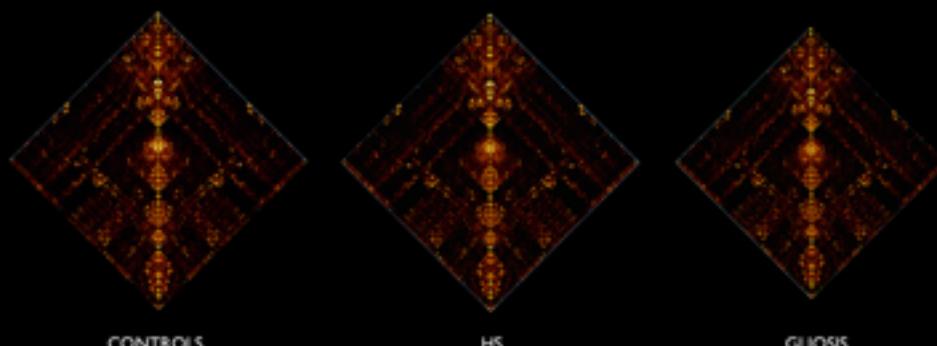


REPRODUCIBILITY AT HIGHER SPATIAL SCALE

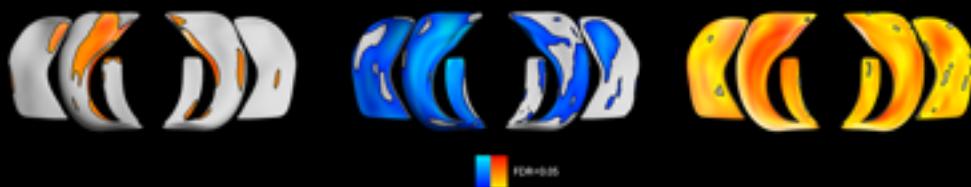
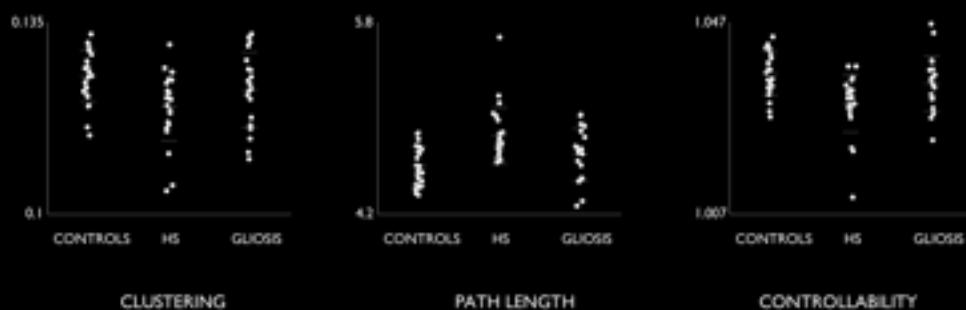
A AAL SUBPARCELLATION



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

AUTISM SPECTRUM DISORDER

COMMON
NEURODEVELOPMENTAL DISORDER

PERSISTS UNTIL ADULTHOOD

CORE DEFICITS
IN SOCIAL COGNITION AND
COMMUNICATION

DIAGNOSIS AND THERAPY CHALLENGED
BY CONSIDERABLE HETEROGENEITY



PREVIOUS STRUCTURAL MRI WORK

INCONSISTENT LOCATION OF FINDINGS
INCONSISTENT DIRECTION
MIXED INCLUSION CRITERIA
VARIABLE AGE RANGES
ONLY SMALL SAMPLES STUDIED



Available online at www.sciencedirect.com



European Psychiatry 23 (2008) 289–299

EUROPEAN
PSYCHIATRY

<http://www.sciencedirect.com/science/ELSYPSY/>

Review

Towards a neuroanatomy of autism: A systematic review and meta-analysis of structural magnetic resonance imaging studies

Andrew C. Stanfield ^{a,*}, Andrew M. McIntosh ^a, Michael D. Spencer ^a,
Ruth Philip ^a, Sonia Gaur ^b, Stephen M. Lawrie ^a

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doi:10.1093/brain/awq279

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BRAIN
A JOURNAL OF NEUROLOGY

Age-related temporal and parietal cortical thinning
in autism spectrum disorders

Gregory L. Wallace,¹ Nathan Dankner,¹ Lauren Kenworthy,¹ Jay N. Giedd² and Alex Martin¹



Cerebral Cortex, 2014, 1–13

doi:10.1093/cercor/cwu242
ORIGINAL ARTICLE

ORIGINAL ARTICLE

Anatomical Abnormalities in Autism?

Shlomi Haar¹, Sigal Berman³, Marlene Behrmann⁴, and Ilan Dinstein^{1,2}

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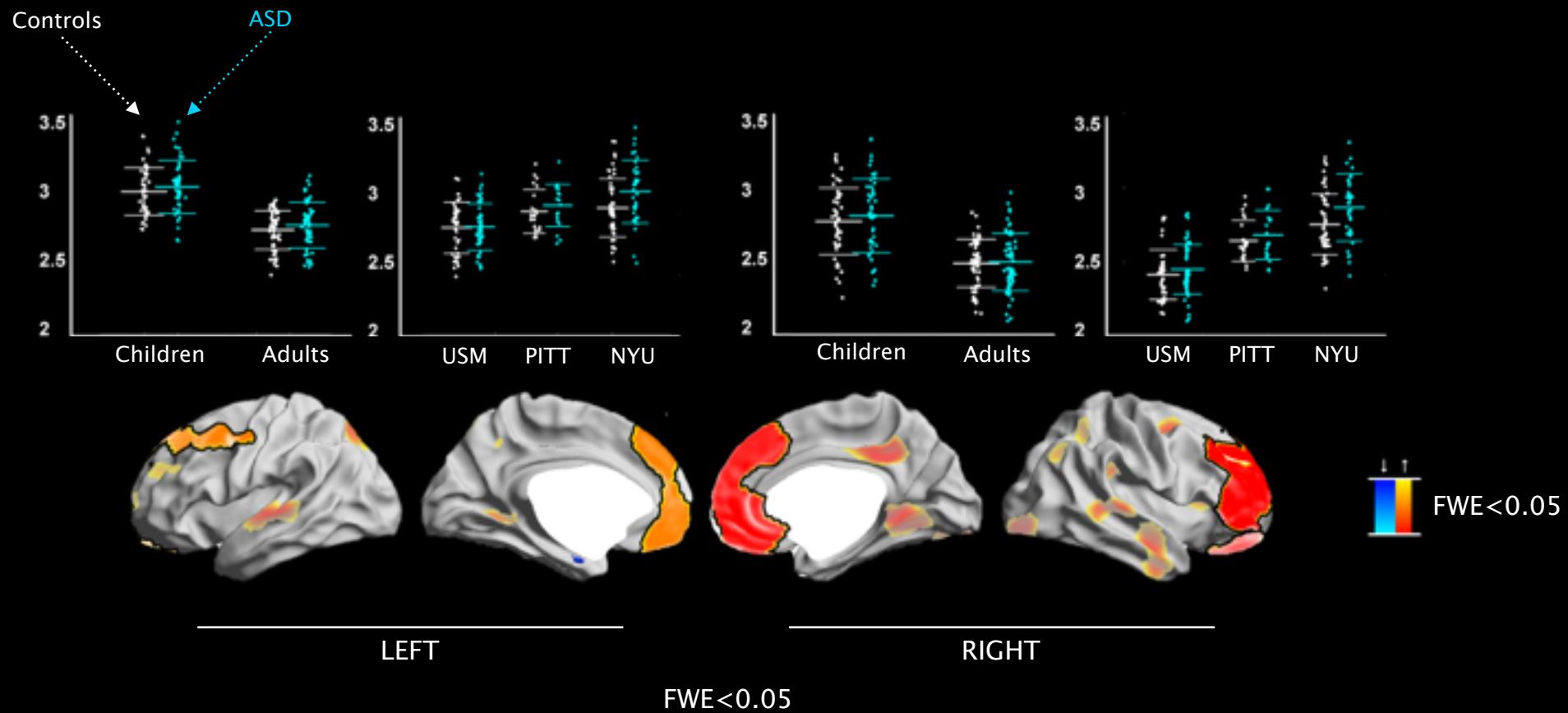
BIG DATA ANALYSIS FOR STRUCTURAL BRAIN ANOMALIES IN AUTISM



FMRI + SMRI + BASIC PHENOTYPING (AGE, SEX, IQ, DIAGNOSTIC)
in 539 ASD and 537 controls
17 sites

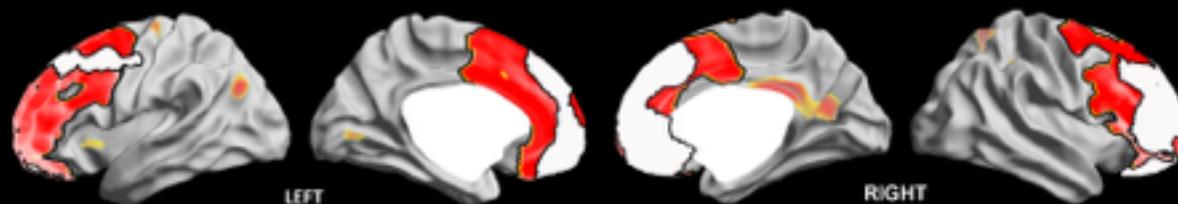
ADOS- and/or ADI-R available in all sites

MULTI-CENTER MAPPING OF STRUCTURAL ALTERATIONS

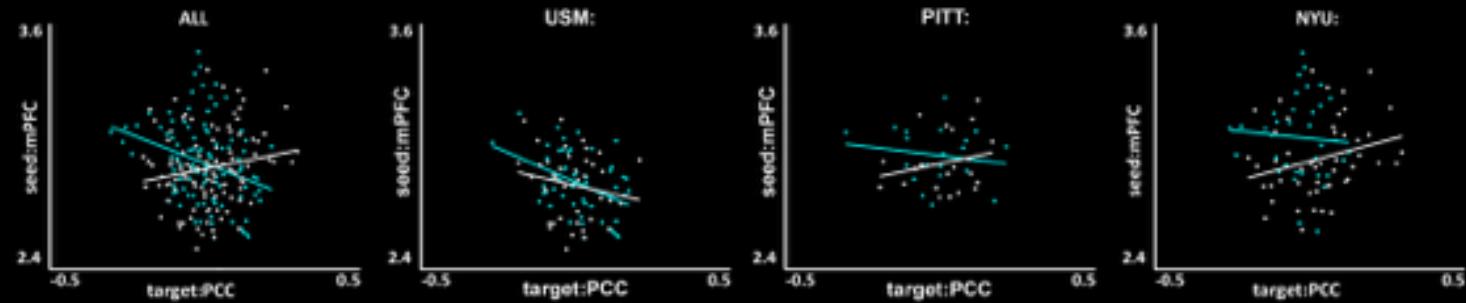
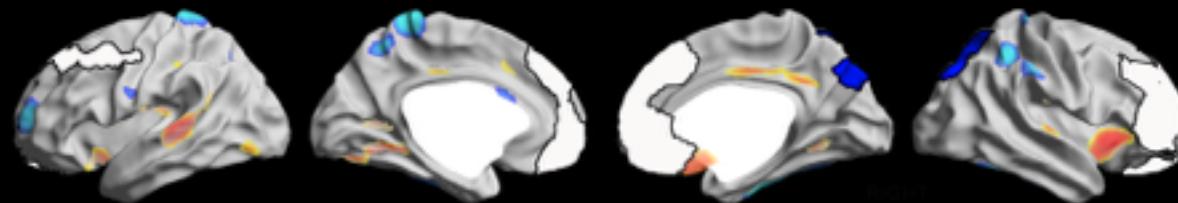


MULTI-CENTER MAPPING OF STRUCTURAL ALTERATIONS

A COVARIANCE NETWORKS IN CONTROLS

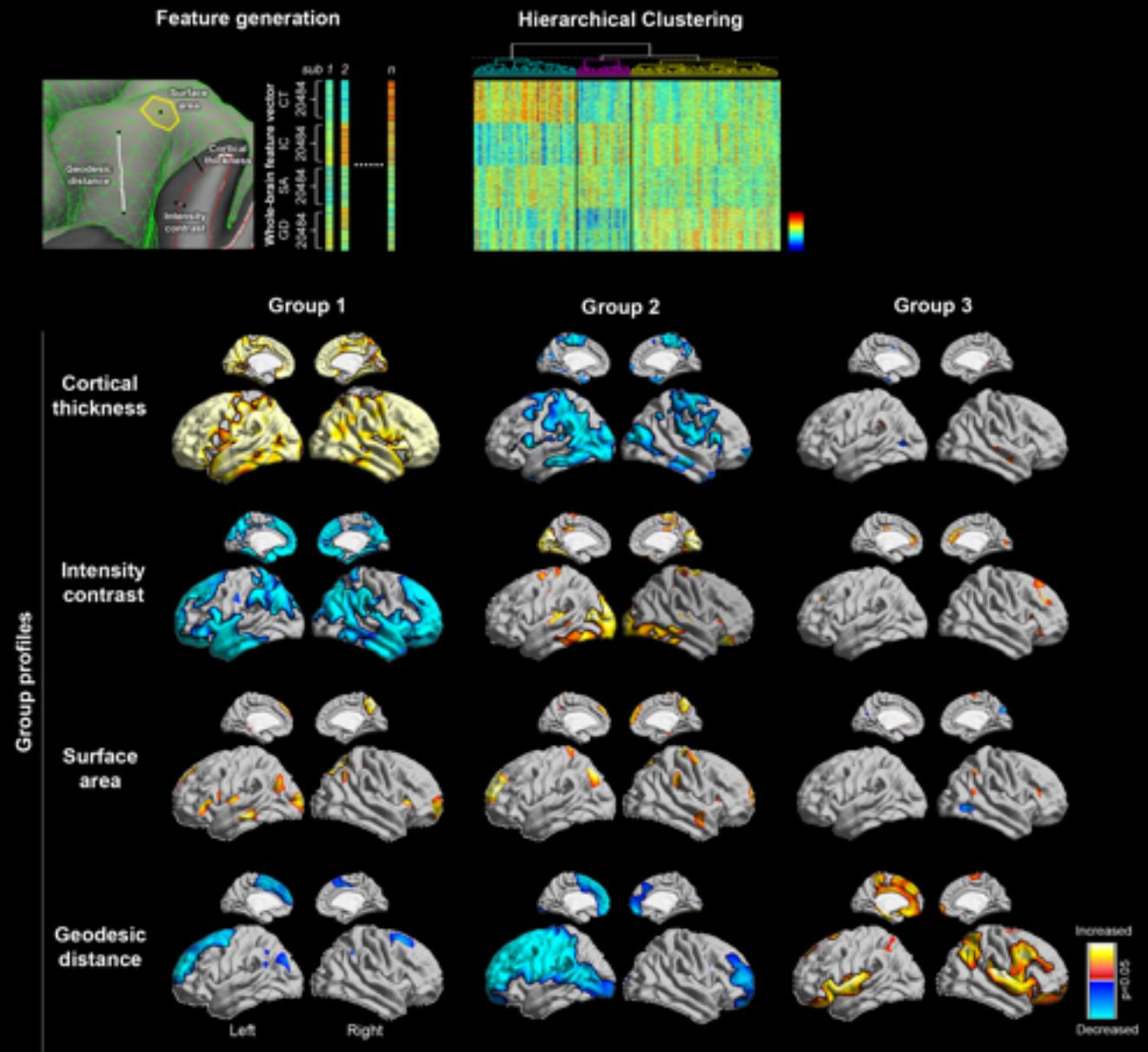


B ALTERATIONS IN ASD



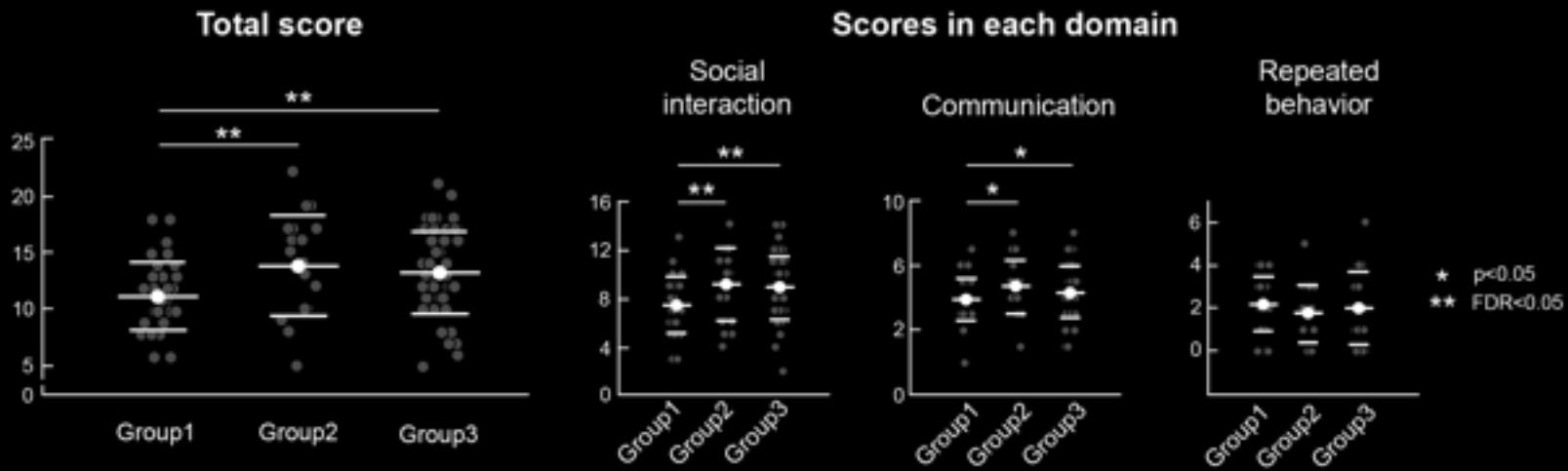
BUT DO MASS-UNIVARIATE GROUP COMPARISONS
ADDRESS HETEROGENEITY WITHIN ASD?

SUBTYPING OF AUTISM SPECTRUM DISORDERS



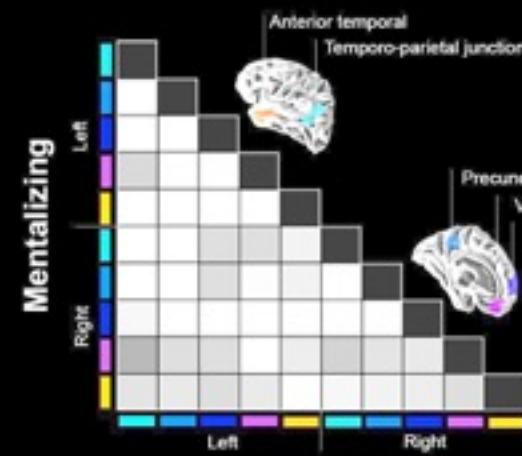
SYMPTOM GRADIENT

ADOS profiles



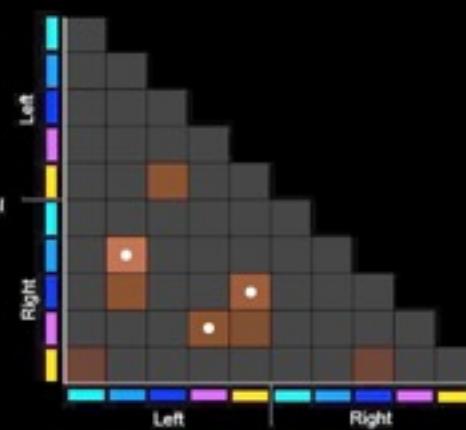
FUNCTIONAL NETWORK ANOMALIES

Functional connectivity in controls

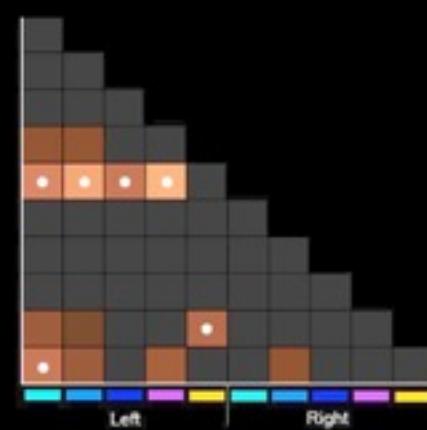


Decreased connectivity in ASD

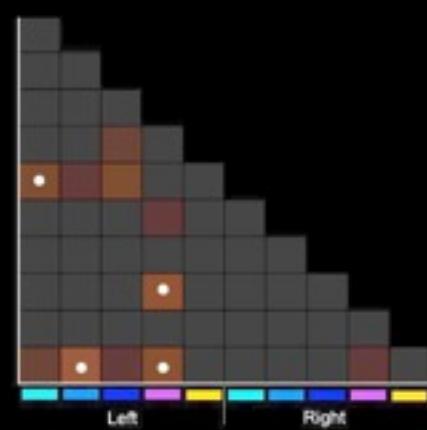
Group 1



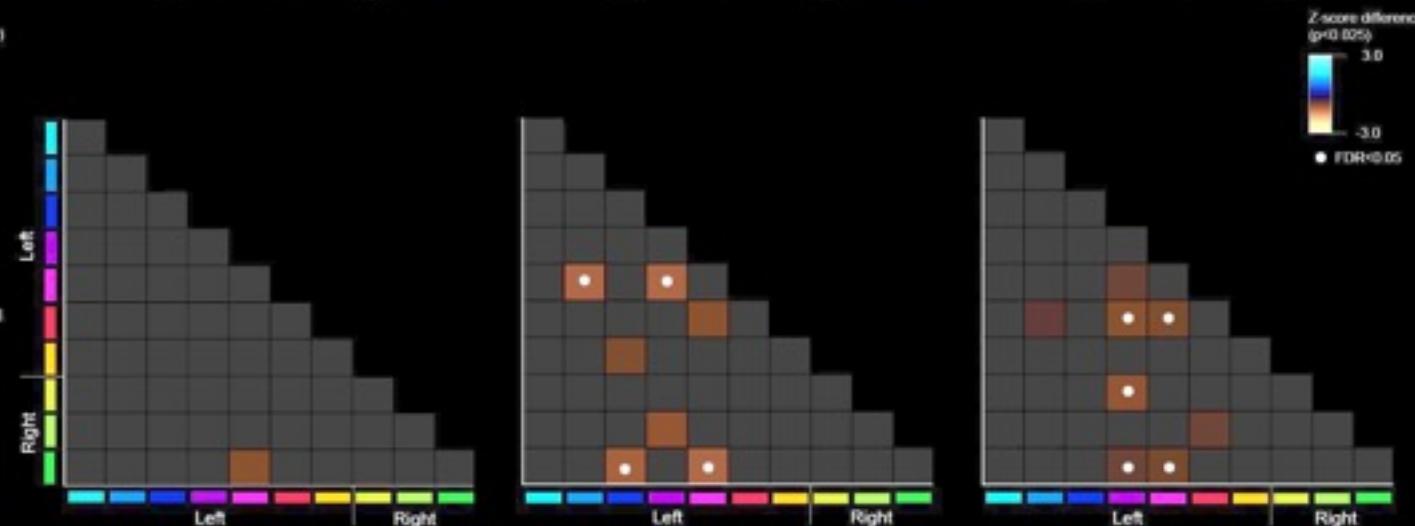
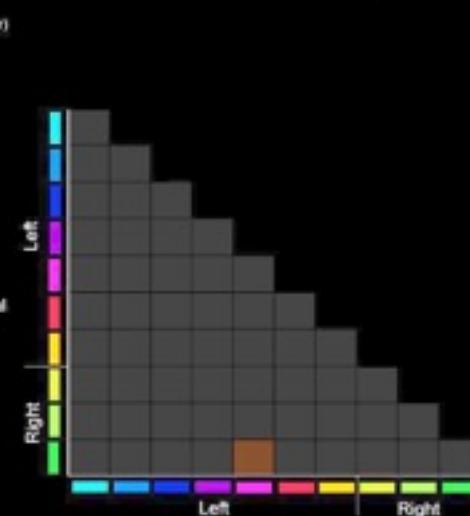
Group 2



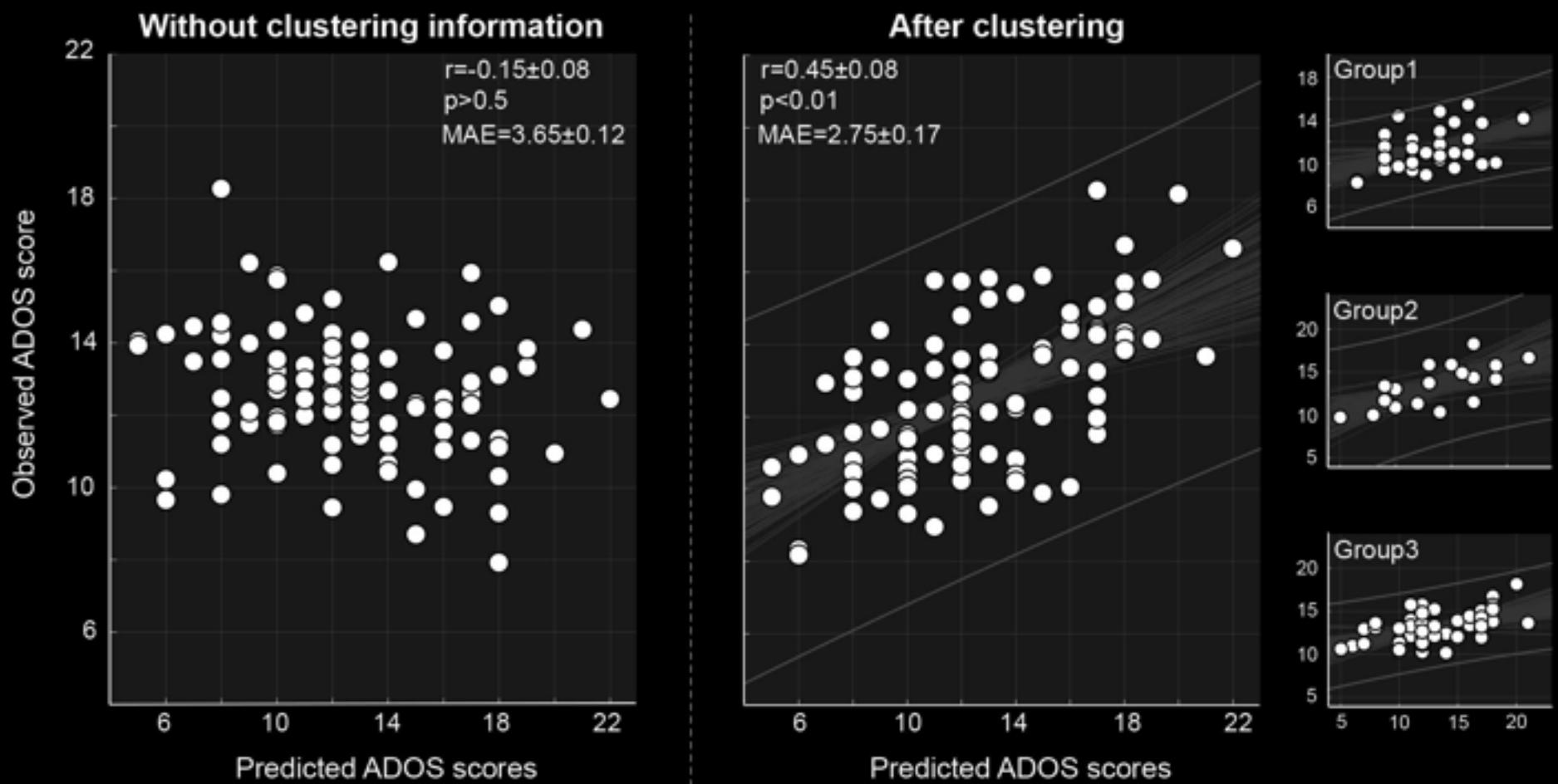
Group 3



Communication



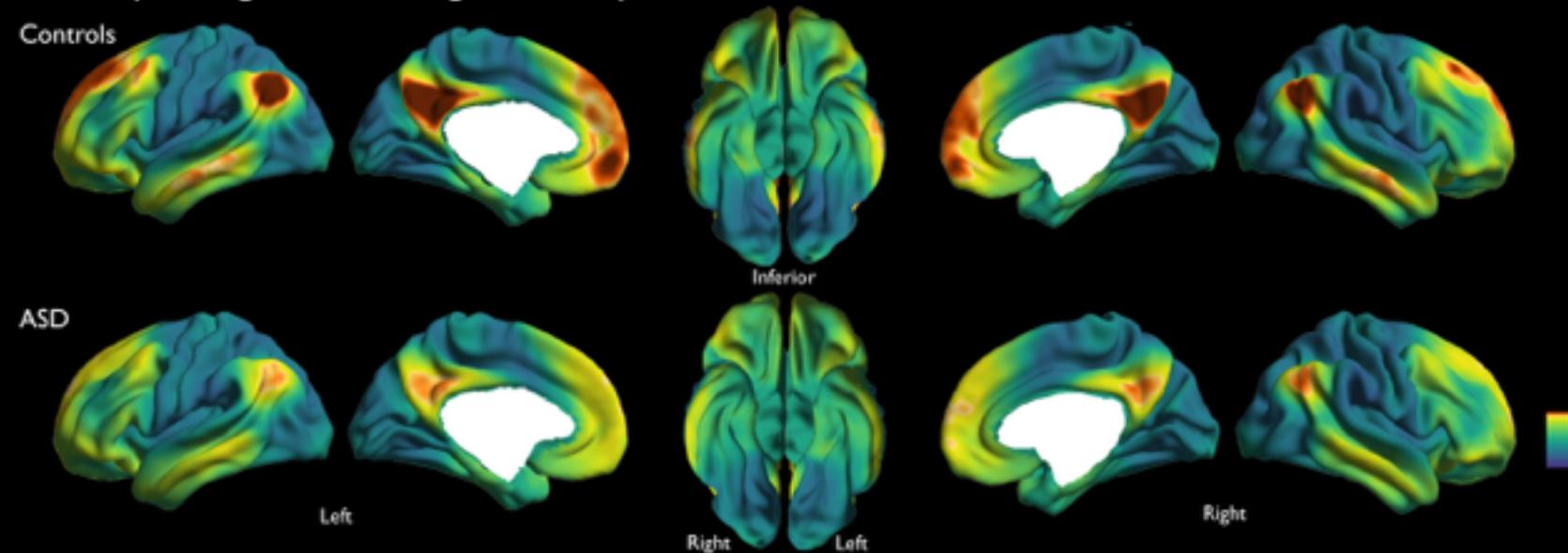
SYMPTOM SEVERITY PREDICTION



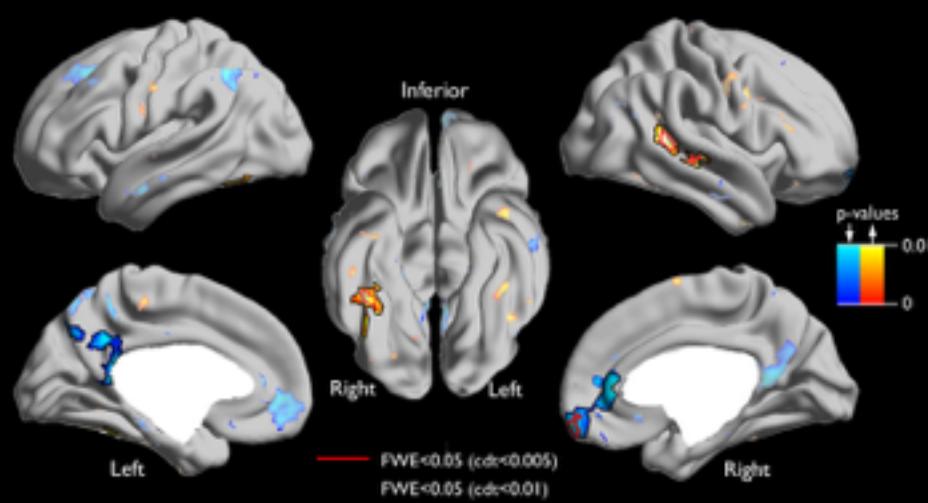
HOW DO STRUCTURAL CHANGES EXTEND TO THE
TO THE CONNECTOME LEVEL?

ALTERED CONNECTOME ORGANIZATION IN AUTISM

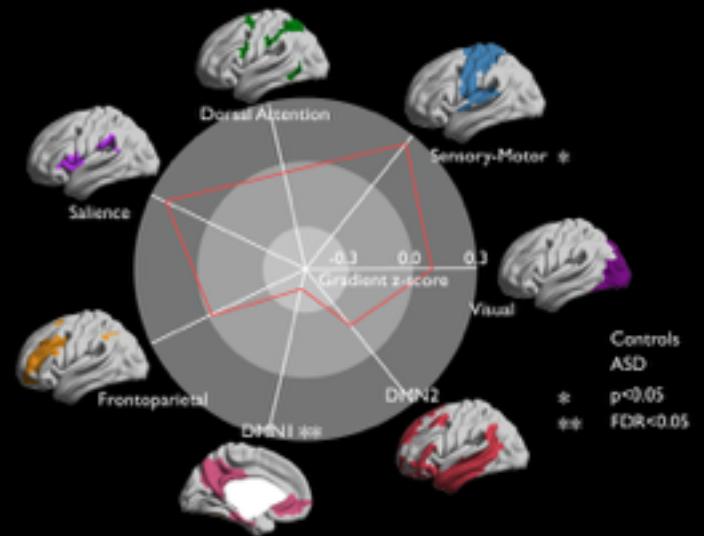
A. Group-averaged functional gradient map



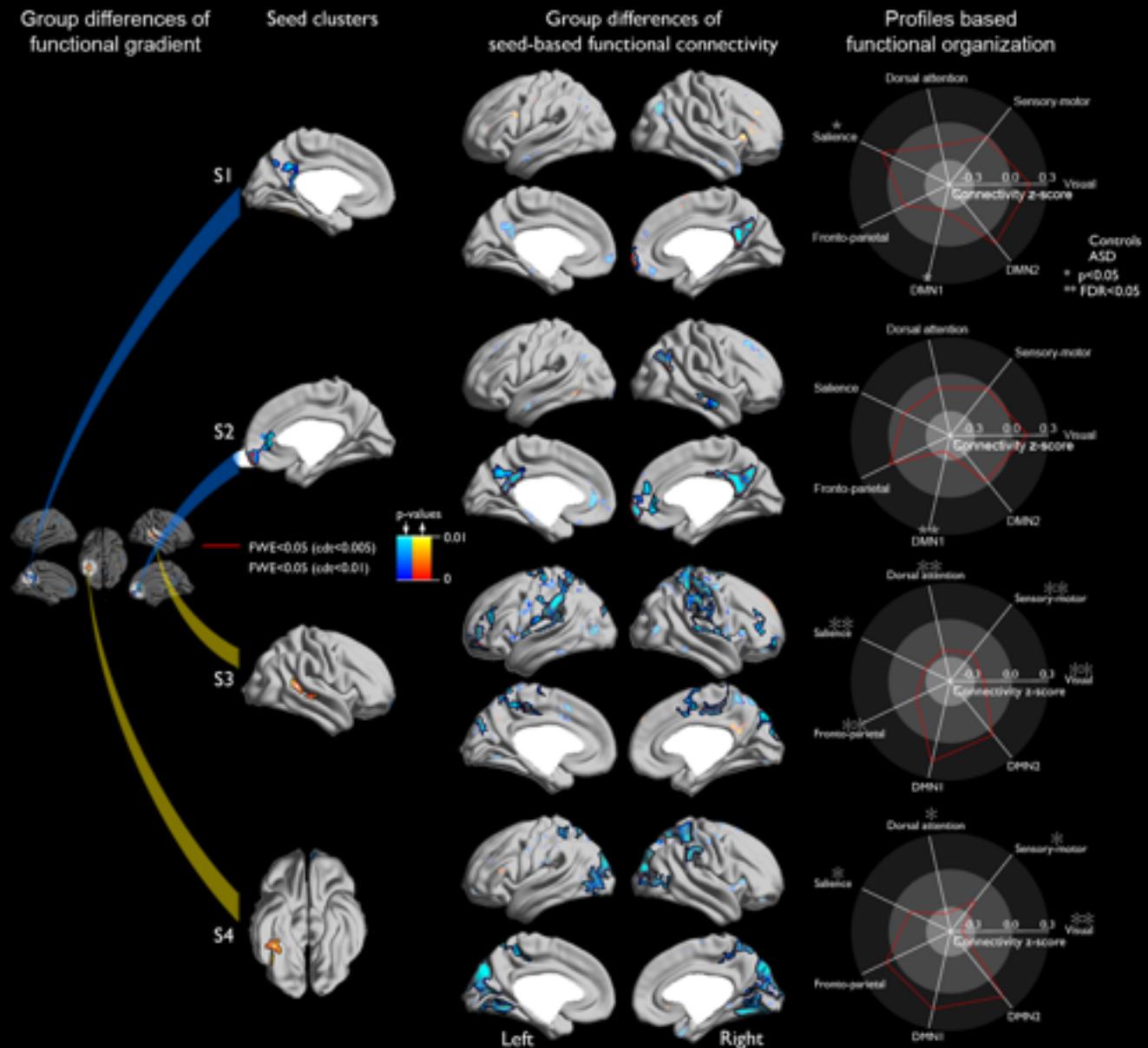
B. Alterations in ASD



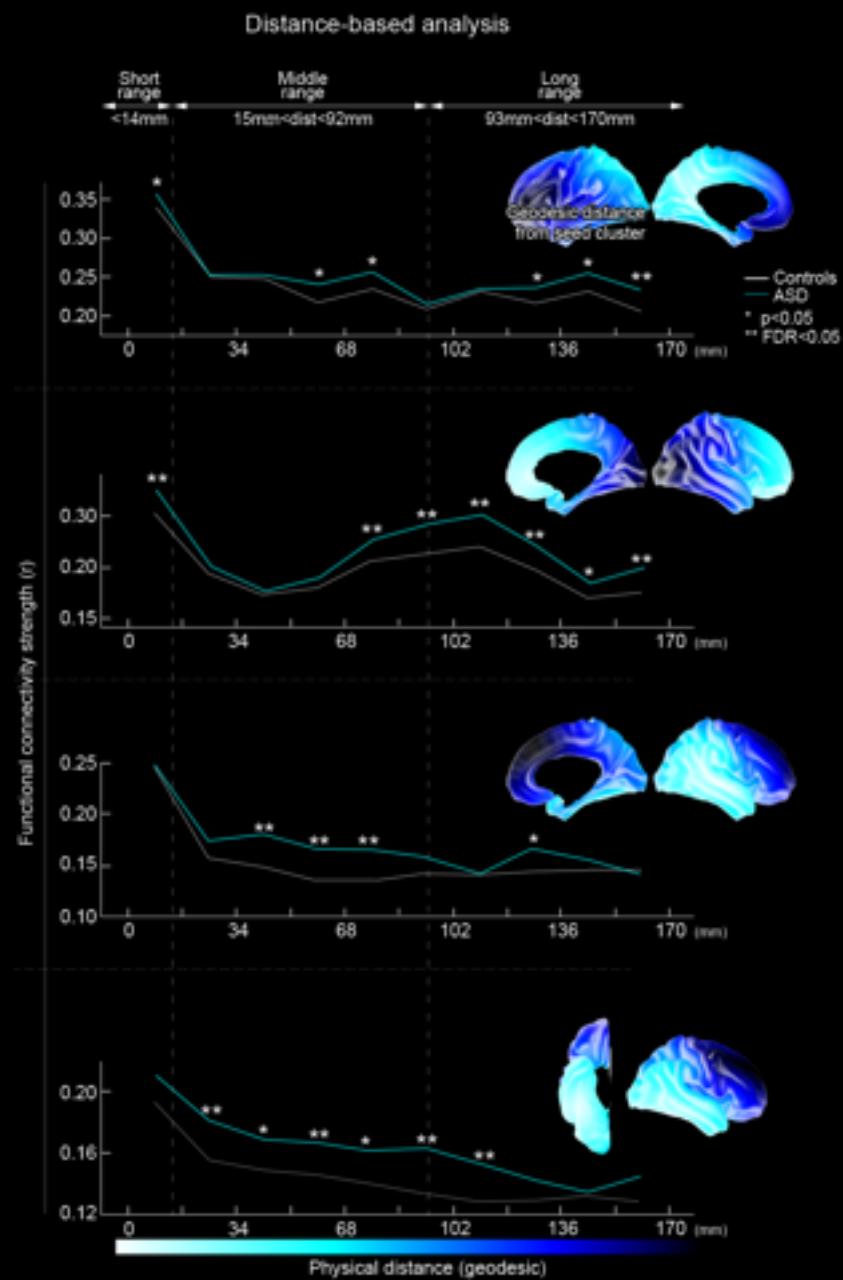
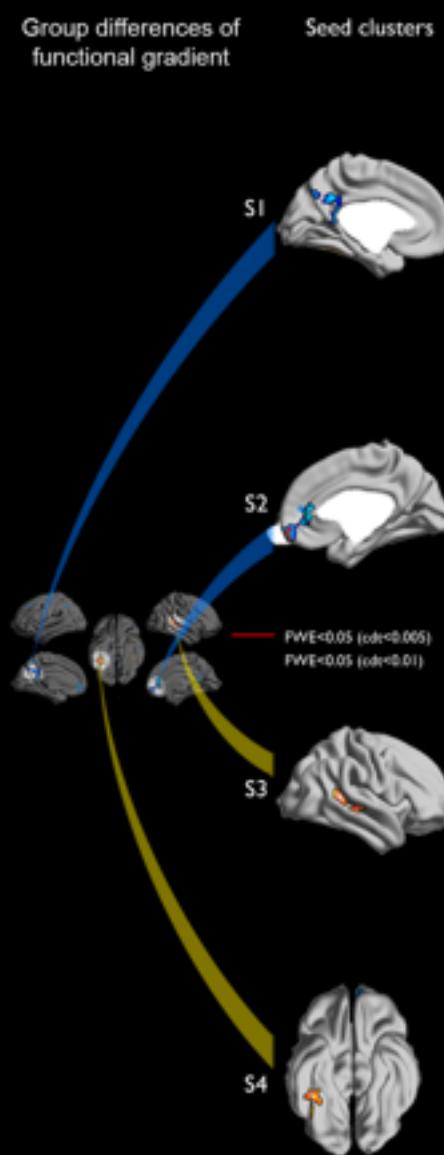
C. Profiling based on functional organization



ALTERED CONNECTOME ORGANIZATION IN AUTISM



ALTERED CONNECTOME ORGANIZATION IN AUTISM



INTERIM SUMMARY: AUTISM

MOVING TOWARDS LARGE DATASETS

BETTER CAPTURE HETEROGENEITY

EVALUATE MULTI-SITE REPRODUCIBILITY

SUBTYPING APPROACHES

CONSOLIDATE PREVIOUS, SOMETIMES NON-CONGRUENT FINDINGS

BENEFITS FOR INDIVIDUALIZED PREDICTION OF SYMPTOM LEVELS

POTENTIALLY USEFUL TO CALIBRATE THERAPY

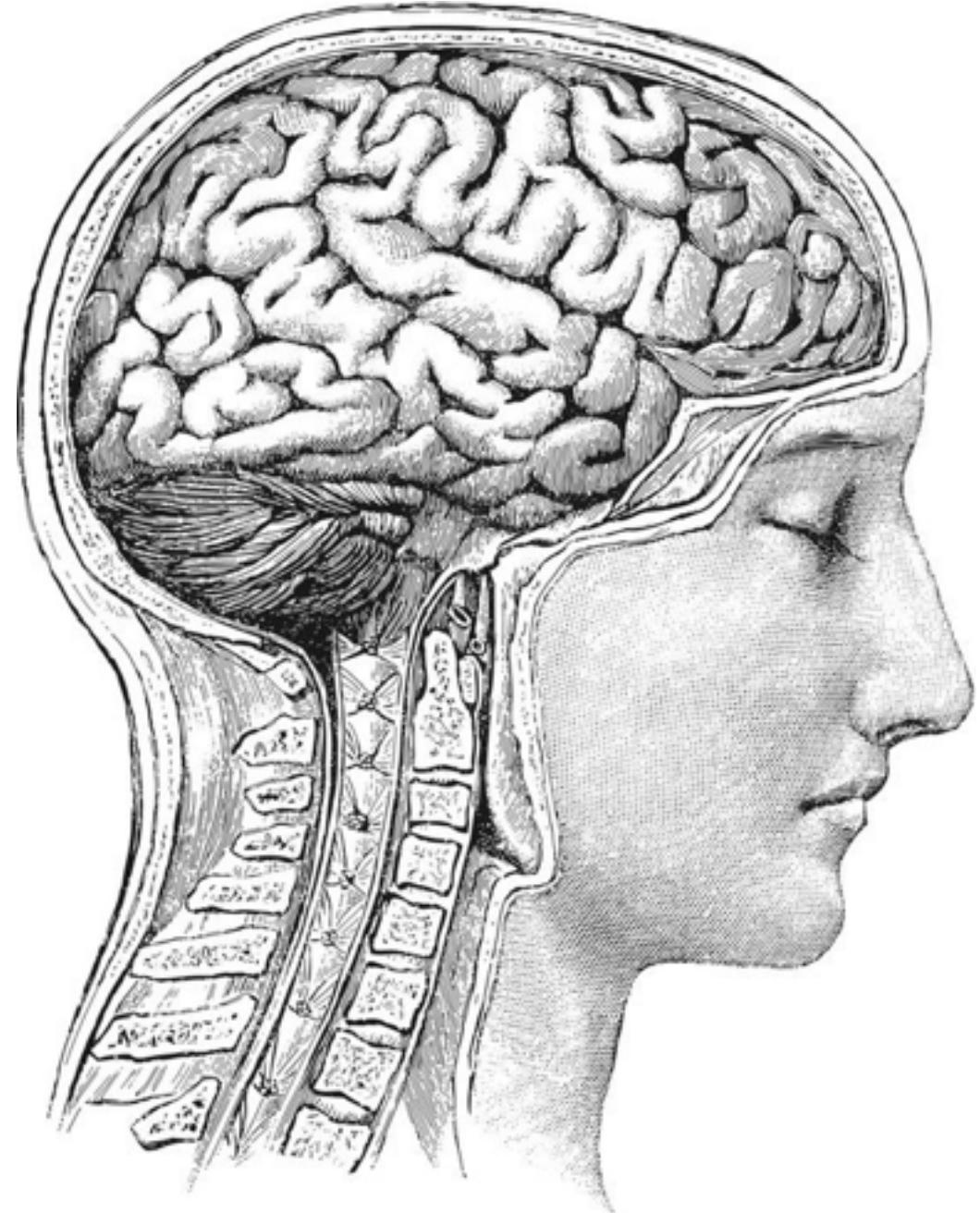
STRUCTURAL ANOMALIES LIKELY TRANSCEND TO CONNECTOME ALTERATIONS

SUMMARY

MRI PROVIDES IN VIVO INFORMATION
ON MICROSTRUCTURE AND
MACROSCALE NETWORKS

INTEGRATE HISTOLOGICAL DATA,
MRI PHENOTYPES, AND CONNECTOME
DATA TO CHARACTERIZE THE IMPACT
OF FOCAL EPILEPSY

DESCRIBE ANATOMICAL HETEROGENEITY
IN AUTISM TO BETTER
UNDERSTAND FUNCTIONAL
AND BEHAVIORAL ANOMALIES





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Andrea Bernasconi

Jessie Kulaga Yoskovitz

Ravnoor Gill

Benoit Caldairou

Min Liu

Jeffrey Hall

Marie Christine Guiot



Sofie Valk

Tania Singer

Alfred Anwander

Daniel Margulies



Together We Will.
TOGETHER WE WILL.



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Seok-Jun Hong

Shahin Tavakol

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