

THE IMPACT OF MESIOTEMPORAL PATHOLOGY ON WHITE MATTER SYSTEMS IN TEMPORAL LOBE EPILEPSY

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CONCEPTUAL KNOWLEDGE

GENERALIZE EXPERIENCE TO
NOVEL SITUATIONS

CONCEPTUAL KNOWLEDGE MAY
WORK SIMILAR TO NAVIGATING IN SPACE
“COGNITIVE MAP”

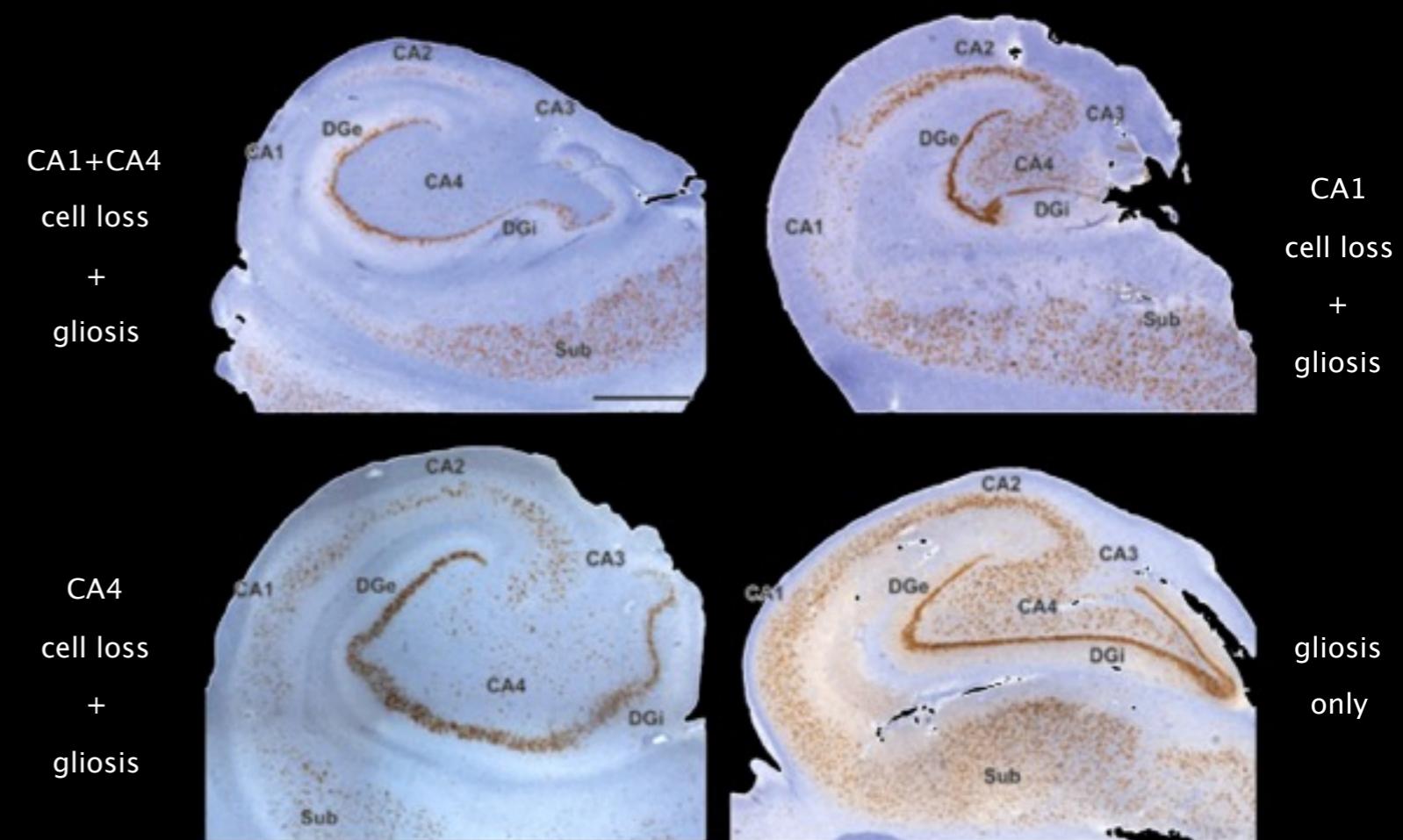
SPATIAL REPRESENTATIONS ARE HEXAGONAL
IN PHG

TEMPORAL LOBE PATHOLOGY

COMMONLY ASSOCIATED WITH
HIPPOCAMPAL SCLEROSIS

HS NOT A UNIFORM ENTITY

VARIABLE CELL LOSS AND/OR GLIOSIS
IN HIPPOCAMPAL SUBFIELDS



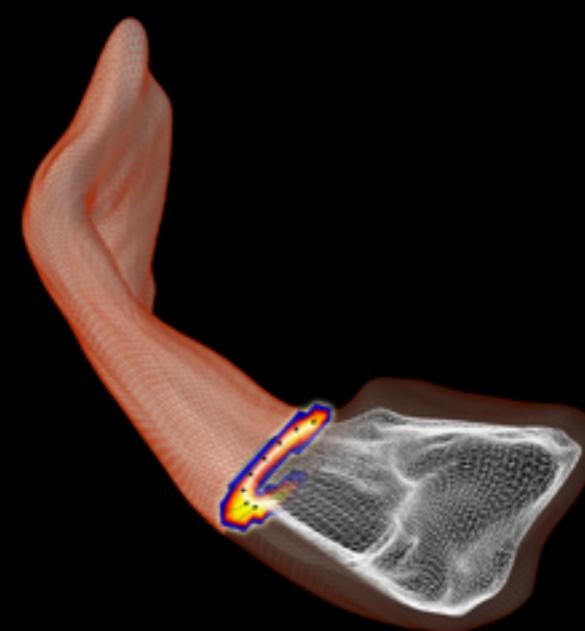
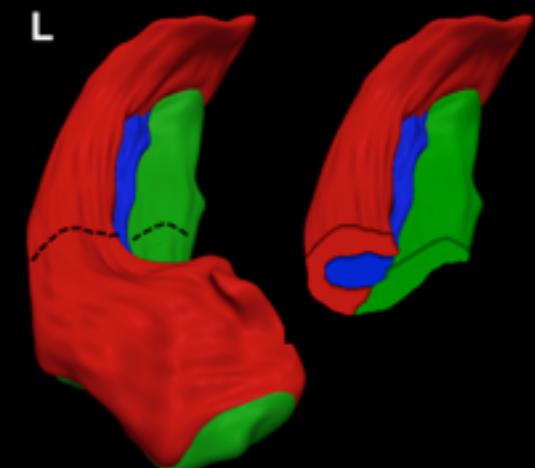
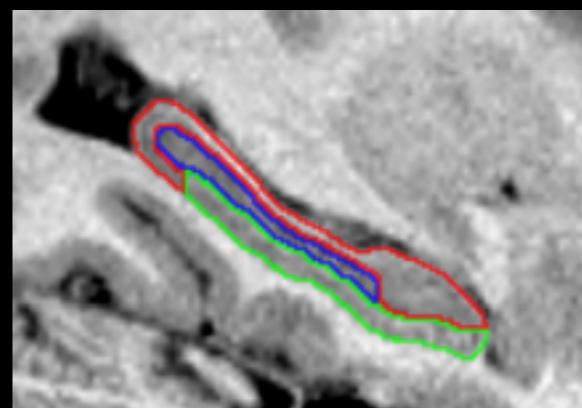
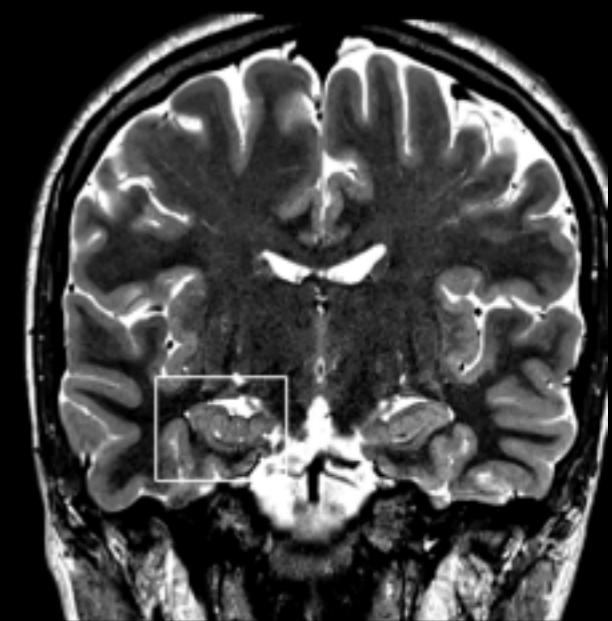
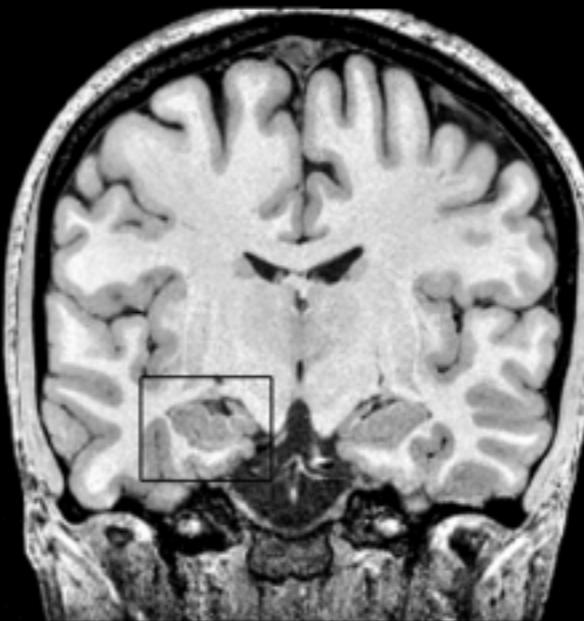
IMAGING OF HS

KEY ROLE OF MRI IN DETECTING
AND DESCRIBING HS

ATROPHY AND T2W

INCREASED SENSITIVITY
WITH SUBFIELD LEVEL DESCRIPTIONS

IN-VIVO FOCUS LATERALIZATION
OUTCOME PREDICTION
PATHOLOGICAL STRATIFICATION



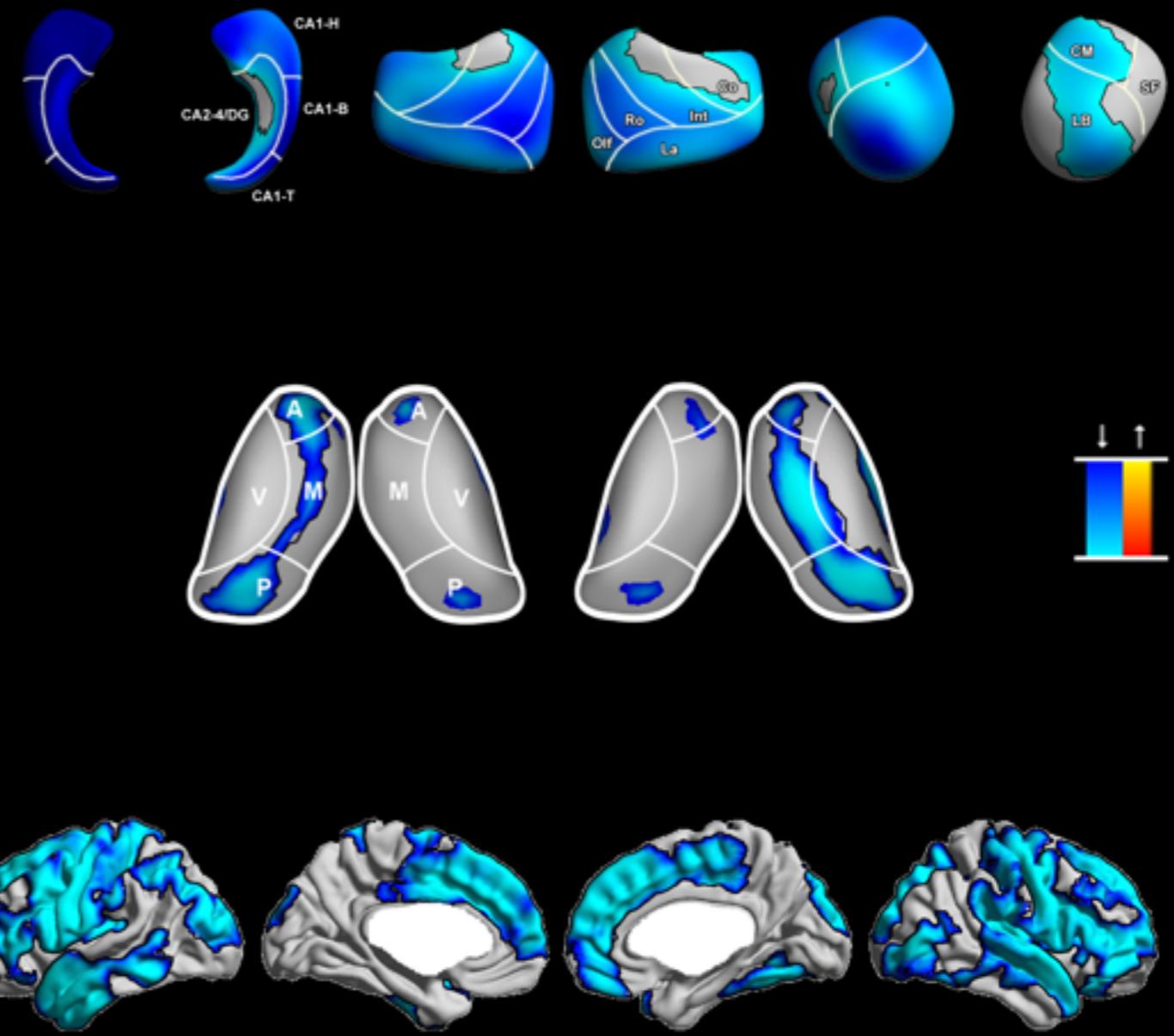
MORE WIDESPREAD GM
CHANGES

MULTIPLE CORTICAL AND SUBCORTICAL
REGIONS AFFECTED

CORTICO-CORTICAL
COVARIANCE NETWORKS ABNORMAL

TLE SYSTEM-LEVEL DISORDER

GREY MATTER COMPROMISE SOMEWHAT
ASSOCIATED WITH DEGREES OF HS



Bonilha et al, Keller et al, Bernasconi et al, Bernhardt et al

WHITE MATTER PATHOLOGY

PATHOLOGICAL REPORTS
POINT TO WM ANOMALIES IN TLE

FINDINGS IN MESIOTEMPORAL WM

DEEP AND SUPERFICIAL WM
BEYOND FOCUS AFFECTED

WM PATHOLOGY STRONGLY ASSOCIATED
WITH THE DEGREE OF HS

TABLE II.—*Ammon's Horn Sclerosis Group with Diffuse and Disseminated Lesions Arranged in Order of Severity. The Various Possible Aetiological Agencies are Given.*

Case and Sex	Age at Onset and Operation	Status at Onset	Grand Mal	Difficult Birth	Other Causes	Side of Lobectomy	Meningeal Fibrosis	Marginal Gliosis	Gyri								Ammon's Horn	Uncus	Amygdaloid			
									Middle		Inferior		Fusiform		Hippoc.							
									C	W	C	W	C	W	C	W						
Esh. F	4 13	—	+	+	Hemiplegia following measles	L.	○	■	▲	■	■	■	■	■	■	■	■	■	■			
Man. F	11 25	+	+	+	Meningitis at 11/12	L.	○○	■	■	■	■	■	■	■	■	■	■	■	■			
Ren. F	2 13	+	+	+	—	L.	○○	■	■	■	■	■	■	■	■	■	■	■	■			
Nob. F	4 18	+	+	—	Teething convulsions 2 years	L.	○○	■	■	■	■	■	■	■	■	■	■	■	■			
Pat. M	3 13	—	—	—	Head trauma 8 years	L.	▲	■	■	■	■	■	■	■	■	■	■	■	■			
Lov. M	3 11	+	+	—	—	L.	■	■	■	■	■	■	■	■	■	■	■	■	■			
Gam. F	8 18	—	—	—	—	L.	▲	■	■	■	■	■	■	■	■	■	■	■	■			
Nev. M	9 16	—	—	—	—	R.	▲	■	■	■	■	■	■	■	■	■	■	■	■			
Joh. F	2 21	+	—	—	Status at 23/12	R.	○	■	■	■	■	■	■	■	■	■	■	■	■			
Wal. M	2 22	—	—	—	—	R.	■	■	■	■	■	■	■	■	■	■	■	■	■			
Har. M	2 36	—	—	—	—	R.	▲	■	■	■	■	■	■	■	■	■	■	■	■			
And. F	1 23	—	—	—	Whooping cough 1/12 before status	L.	■	■	■	■	■	■	■	■	■	■	■	■	■			
Tur. E. F	2 22	—	—	—	Teething convulsions	L.	▲	■	■	■	■	■	■	■	■	■	■	■	■			
Pri. M	2 23	+	+	—	—	R.	▲	■	■	○	○	○	○	○	○	○	○	○	○			
Tur. J. F	14 20	+	+	+	—	L.	▲	■	■	■	■	■	■	■	■	■	■	■	■			
Chu. M	40 49	—	—	—	—	L.	■	■	■	■	■	■	■	■	■	■	■	■	■			
Ric. M	2 32	—	—	—	—	L.	■	■	■	■	■	■	■	■	■	■	■	■	■			
Mac. M	2 45	+	+	+	Status compl. Ch. pox	R.	○	■	■	■	■	■	■	■	■	■	■	■	■			
Kev. F	4/12 43	+	+	—	—	L.	○	▲	○	○	○	○	○	○	○	○	○	○	○			

■ = ++Severity. ▲ = +Severity. □ = Doubtful lesion. ○ = No abnormality. N.A. = Not available. C = Cortex. W = White matter.

TABLE III.—*Group with Minimal Lesions and no Ammon's Horn Sclerosis Arranged in Order of Severity and Showing Possible Aetiological Factors*

Case and Sex	Age at Onset and Operation	Status at Onset	Grand Mal	Difficult Birth	Other Causes	Side of Lobectomy	Meningeal Fibrosis	Marginal Gliosis	Gyri								Ammon's Horn	Uncus	Amygdaloid			
									Middle		Inferior		Fusiform		Hippoc.							
									C	W	C	W	C	W	C	W						
Lee	M 8 38	—	—	—	—	L.	○○	■	□	▲	□	○	○	○	○	○	○	N.A.	N.A.			
Str. F	2 21	—	—	—	Boxer	L.	○○	■	○	○	○	○	○	○	○	○	○	○	○			
Par. M	18 25	—	—	—	—	R.	○○	■	○	○	○	○	○	○	○	○	○	○	○			
You. F	13 45	—	—	—	Head injury at 13 years	L.	○	▲	○	○	○	○	○	○	○	○	○	○	○			
Cha. F	16 27	—	—	—	Wh. cough at 2½ years	R.	▲	▲	□	○	○	○	○	○	○	○	N.A.	N.A.	○			
Tay. M	14 27	—	—	—	Sinusitis at 16 years	L.	○	▲	○	○	○	○	○	○	○	○	○	○	○			
Par. M	18 25	—	—	—	T.B. hip with meningismus at 12 years	L.	○	▲	○	○	○	○	○	○	○	○	○	○	○			
Fau. M	18 45	—	—	—	Otitis media	L.	○	▲	○	○	○	○	○	○	○	○	○	○	○			
					Head injury at 18 years	R.	○	□	○	○	○	○	○	○	○	○	○	○	○			

■ = ++Severity. ▲ = +Severity. □ = Doubtful lesion. ○ = No abnormality. N.A. = Not available. C = Cortex. W = White matter.

PROBING THE WM WITH DIFFUSION MRI

DIFFUSION PARAMETERS PROBE
TISSUE/ARCHITECTURE

TRACTOGRAPHIC DELINEATION OF
WM TRANSPORT SYSTEMS

CONNECTOME ANALYSIS OF
LARGE-SCALE NETWORKS



Courtesy of Dr Alfred Anwander

DEEP WM FINDINGS

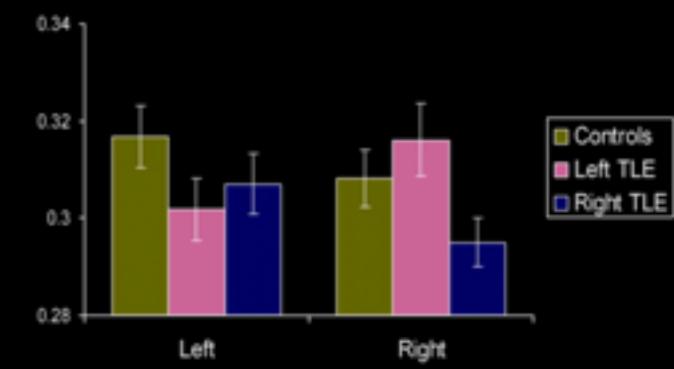
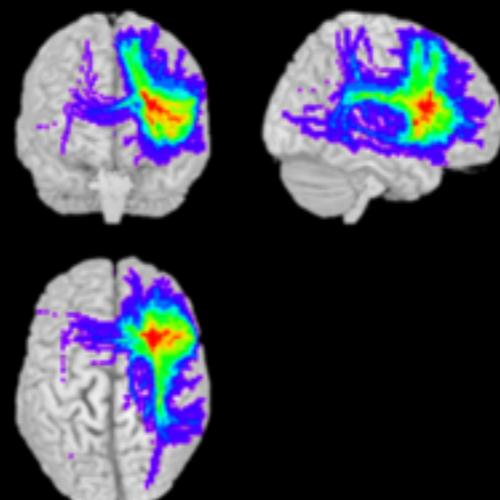
NUMEROUS STUDIES HAVE SHOWN ANOMALIES IN DEEP WM TRACTS

WIDESPREAD PATTERN OF FINDINGS OF FA DECREASES AND MD INCREASES

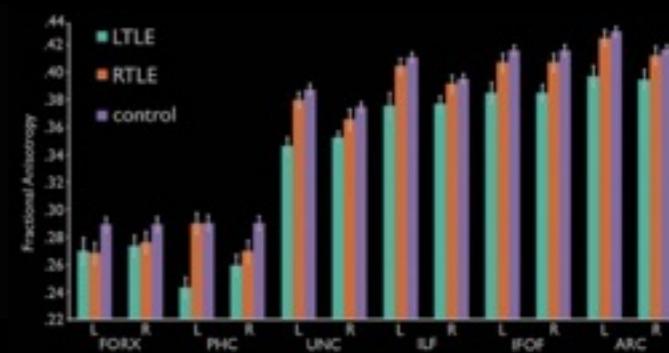
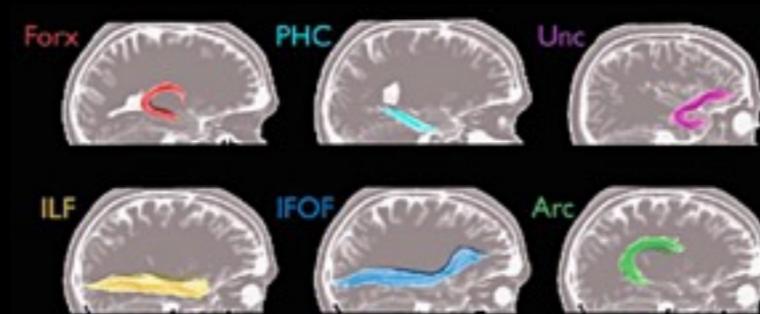
MORE MARKED EFFECTS IN TLE-HS



Concha et al (2005) Ann Neu



Powell et al (2005) Ann Neu

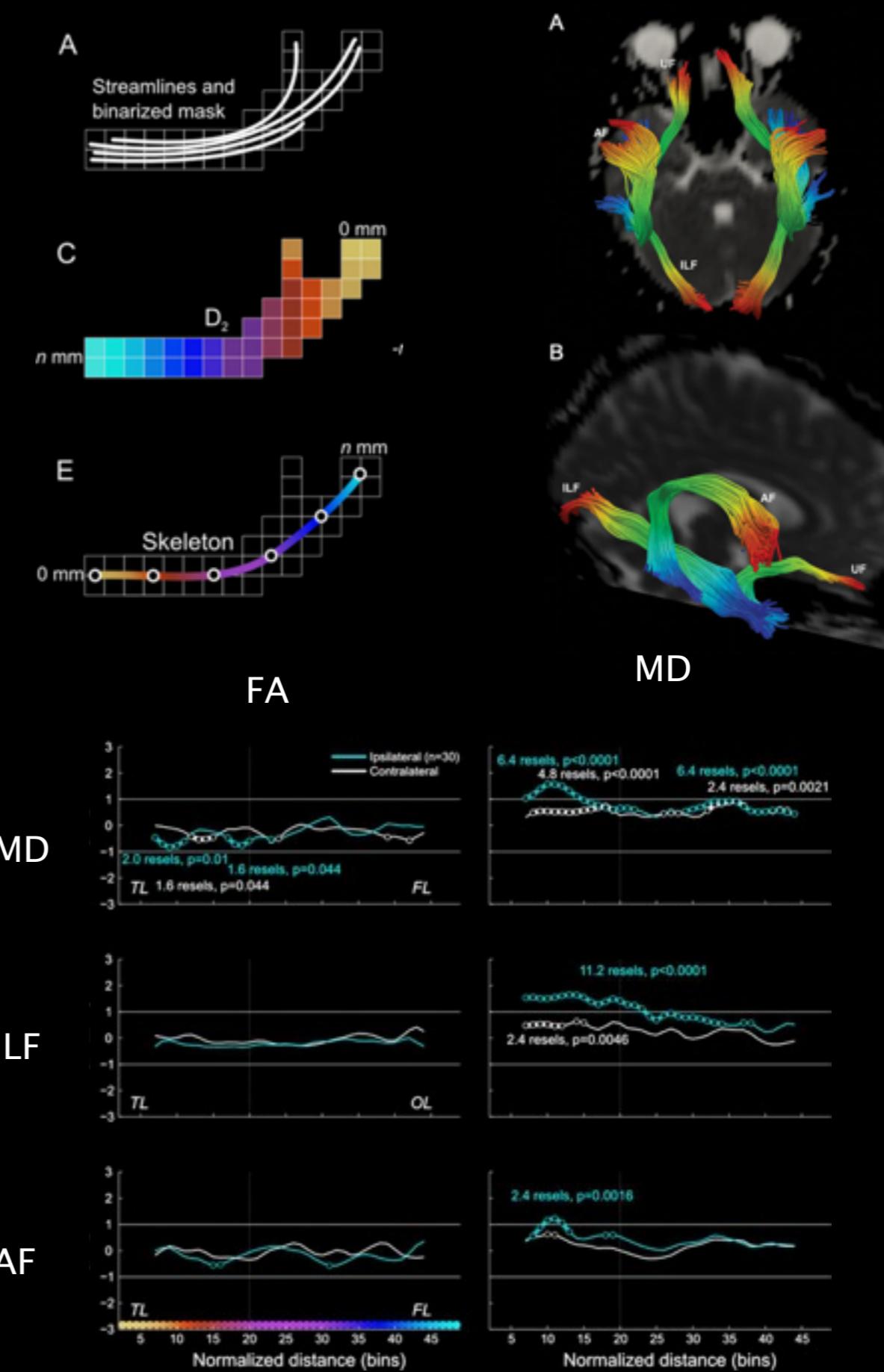


Kemmottuso et al (2011) Epilepsia

DEEP WM FINDINGS

DIFFUSION PARAMETER PROFILING ALONG FIBER TRACTS

ANOMALIES RELATE TO
ANATOMICAL DISTANCE FROM
TEMPORAL LOBE



TODAY'S TALK

SURFACE-BASED ANALYSIS OF THE SUPERFICIAL WHITE MATTER
LINKING HIPPOCAMPAL PATHOLOGY TO FUNCTIONAL NETWORKS

TLE PATHOCONNECTOMICS ARE MODULATED BY
MISSTRUCTURAL VARIATIONS IN HIPPOCAMPAL PATHOLOGY



SURFACE-BASED ANALYSIS OF THE SUPERFICIAL WHITE MATTER LINKING HIPPOCAMPAL PATHOLOGY TO FUNCTIONAL NETWORKS

Liu, Bernhardt, Hong, Caldairou, Bernasconi, Bernasconi



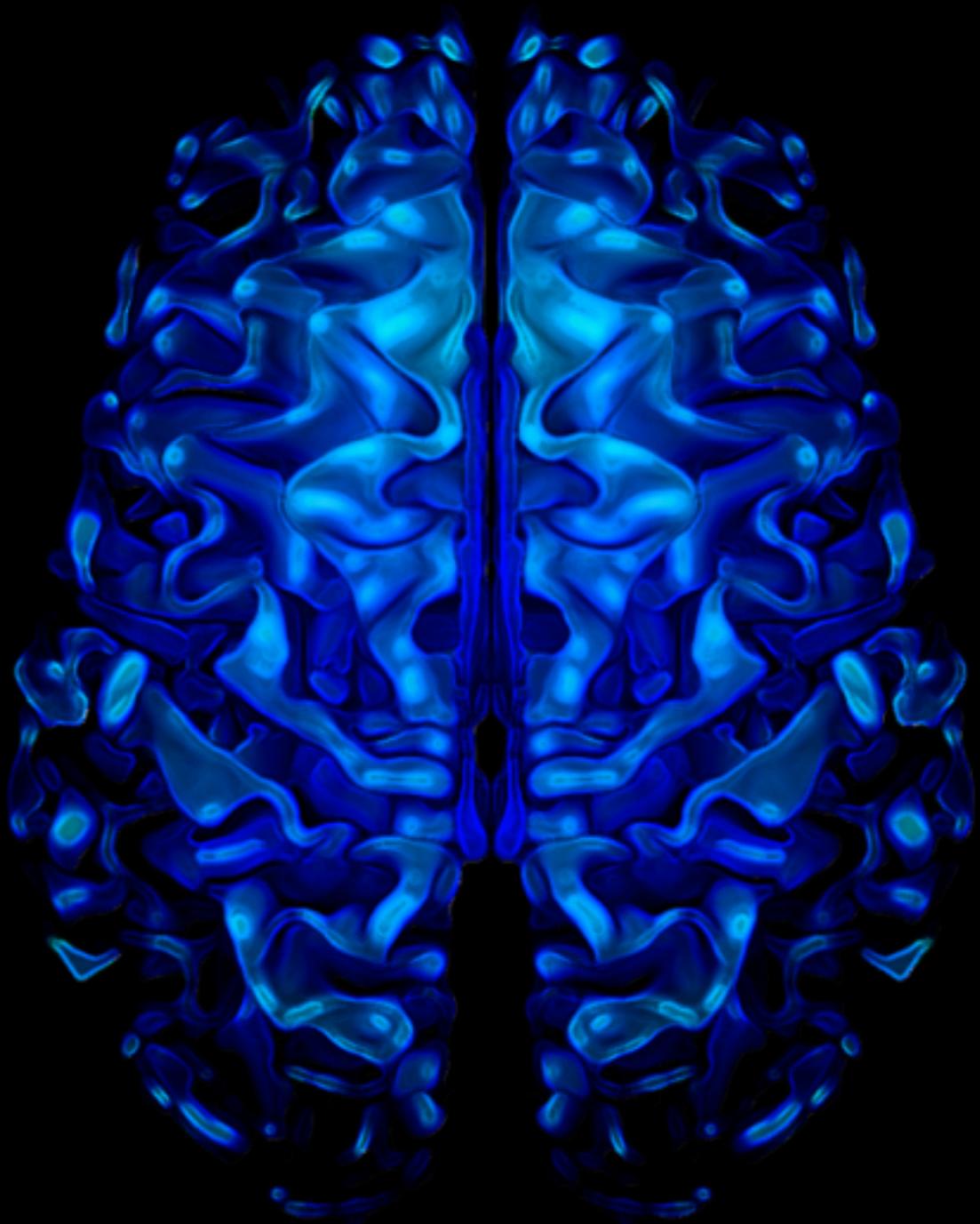
SUPERFICIAL WM

ANOMALIES STUDIED ON PATHOLOGY
BUT RARELY IN VIVO

FINDINGS MAY RELATE TO:
LOCAL GM MORPHOLOGY

ANOMALIES MAY HINDER
INTERREGIONAL CONNECTIVITY

IMPACT ON
LARGE-SCALE FUNCTIONAL NETWORKS



Courtesy of Dr Owen Phillips

METHODS

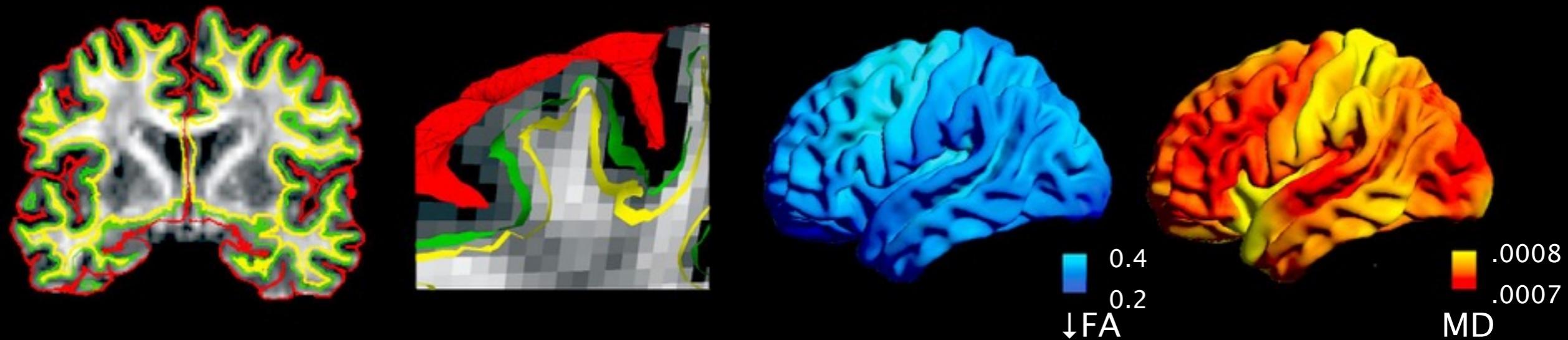
61 TLE PATIENTS (31 LTLE, 30 RTLE)

43 OPERATED, ALL SHOWED EVIDENCE OF HIPPOCAMPAL PATHOLOGY
(15 GLIOISIS ONLY, 28 MARKED HS)

38 AGE-SEX MATCHED CONTROLS

3T IMAGING:
T1-WEIGHTED MRI
DIFFUSION MRI
RESTING-STATE FMRI

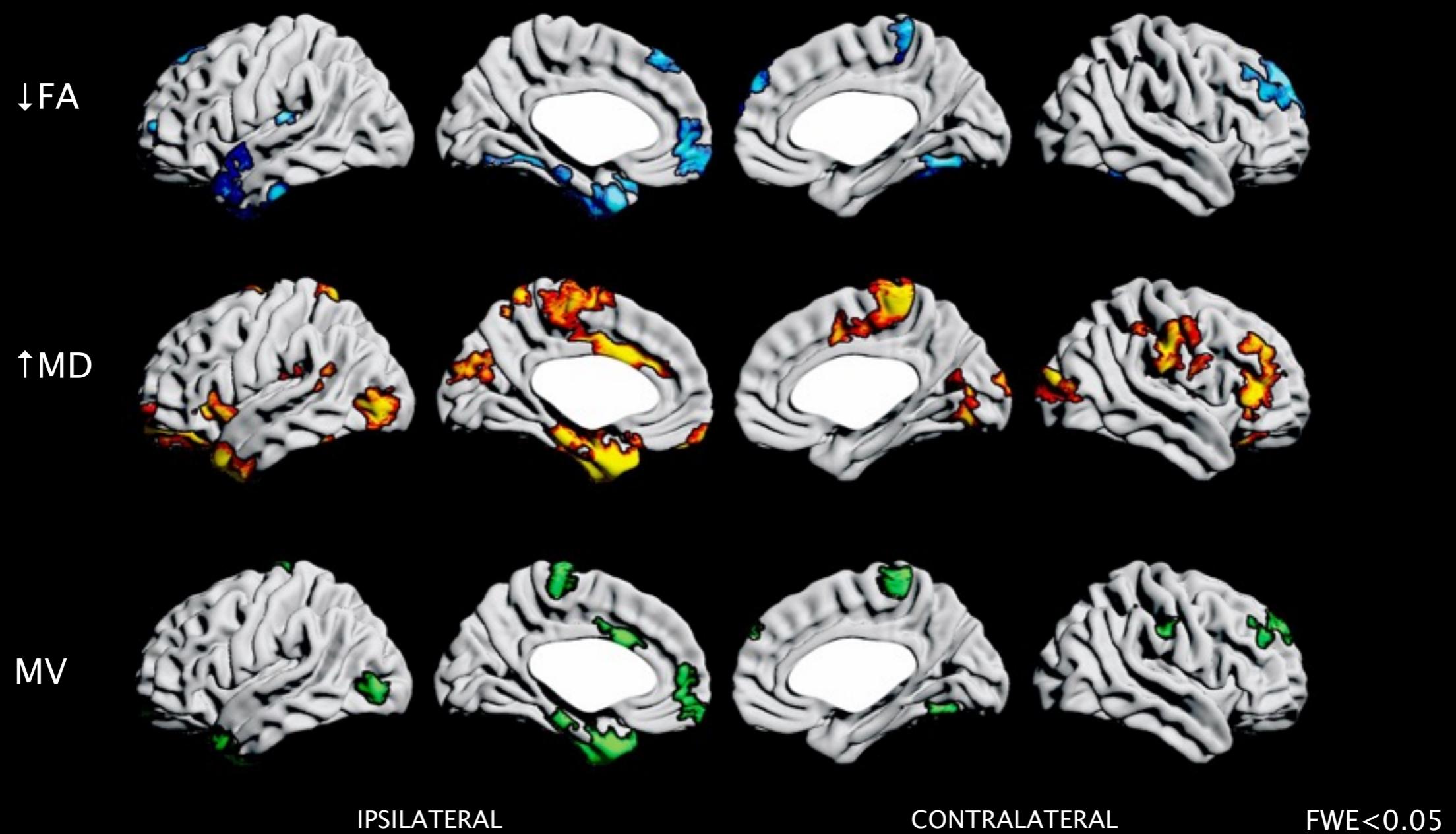
MULTI-PARAMETER ANALYSIS OF SUPERFICIAL WM



SURFACE GENERATION
CROSS-MODAL COREGISTRATION
LAPLACE-GUIDED SURFACE PEELING

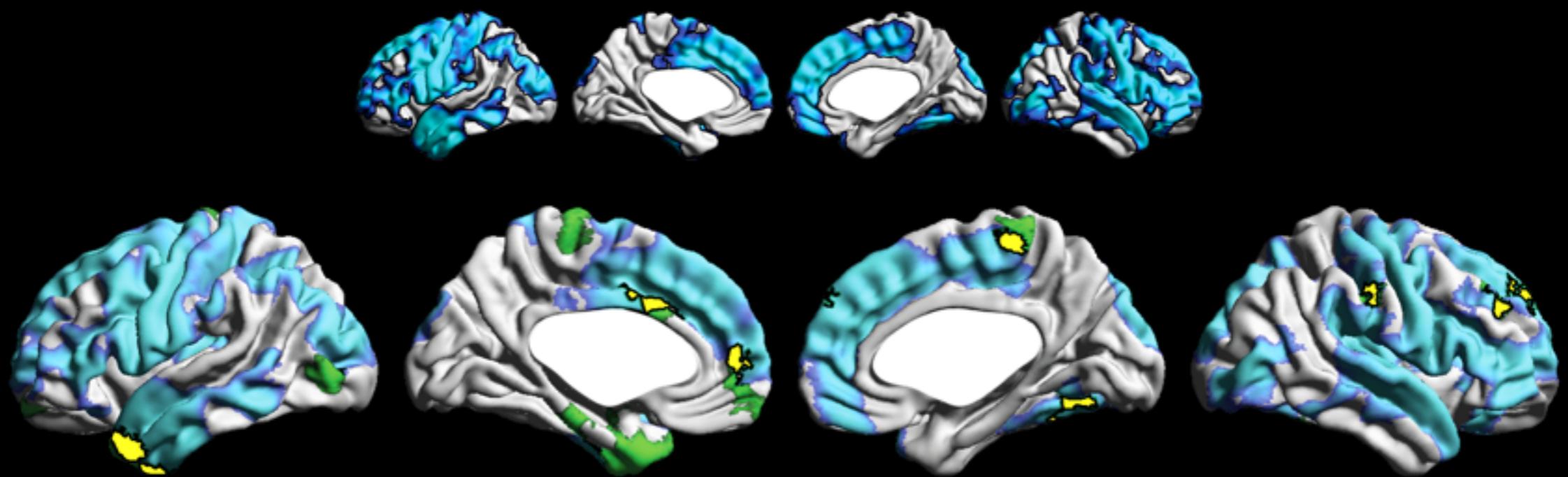
DENSE DTI PARAMETER SAMPLING
BASED ON SUPERFICIAL WM SURFACES
CROSS-SUBJECT CO-REGISTRATION

MULTI-PARAMETER ANALYSIS OF SUPERFICIAL WM



INDEPENDENCE FROM CORTICAL THINNING

CORTICAL THINNING

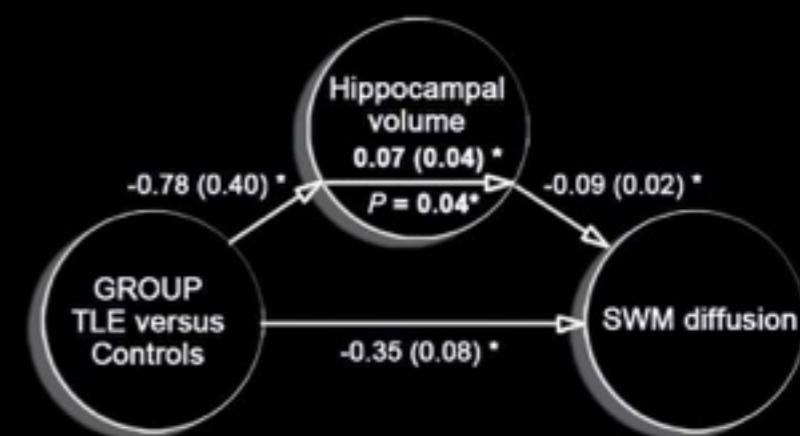
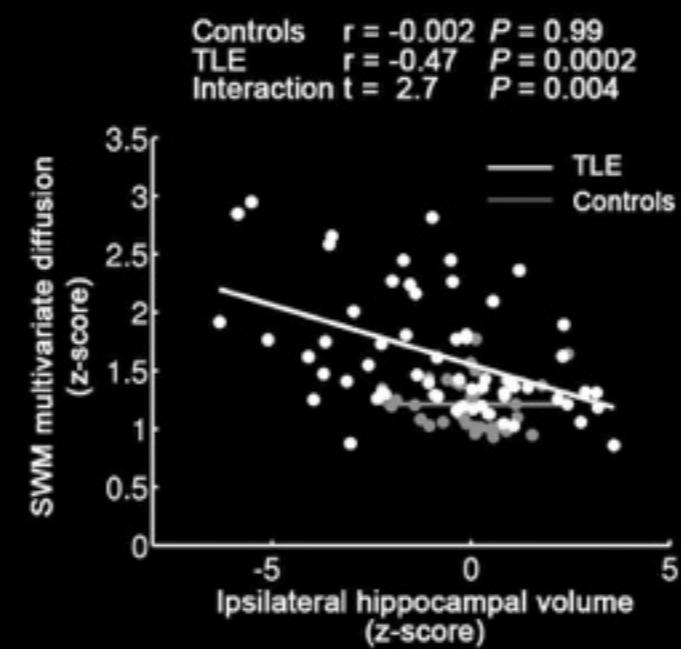
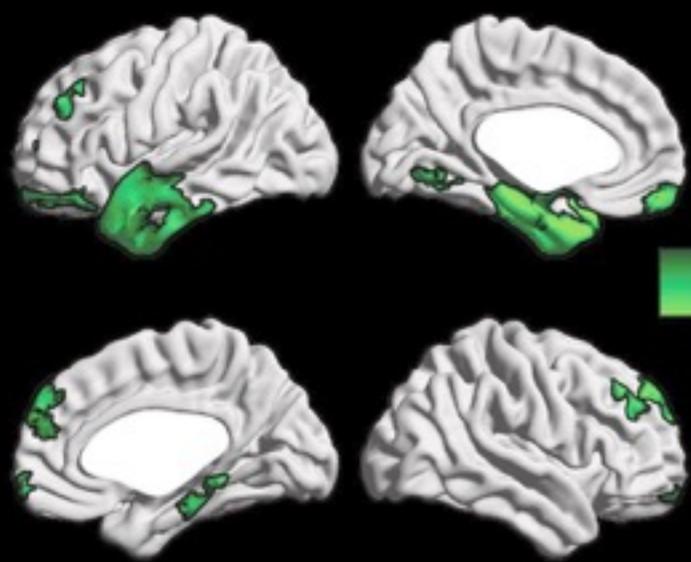


■ CTX

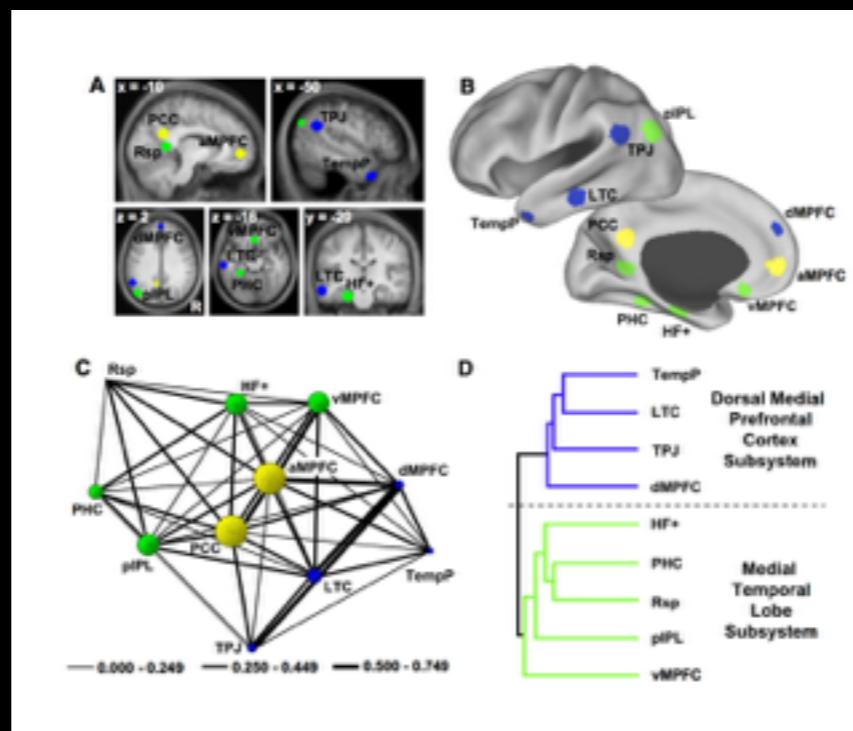
■ DWI

■ BOTH

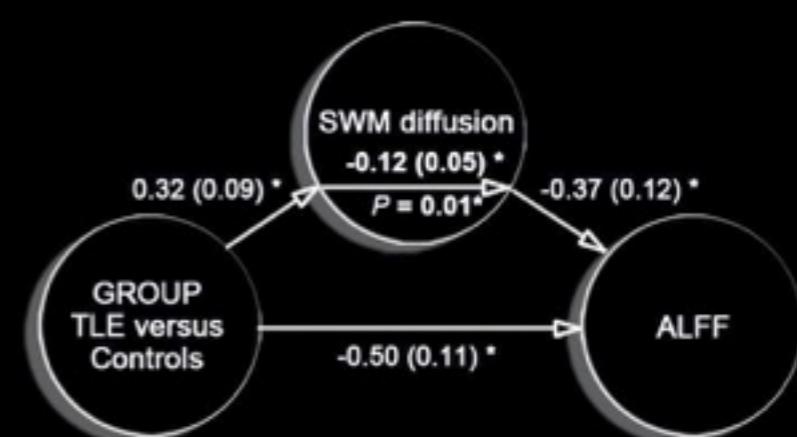
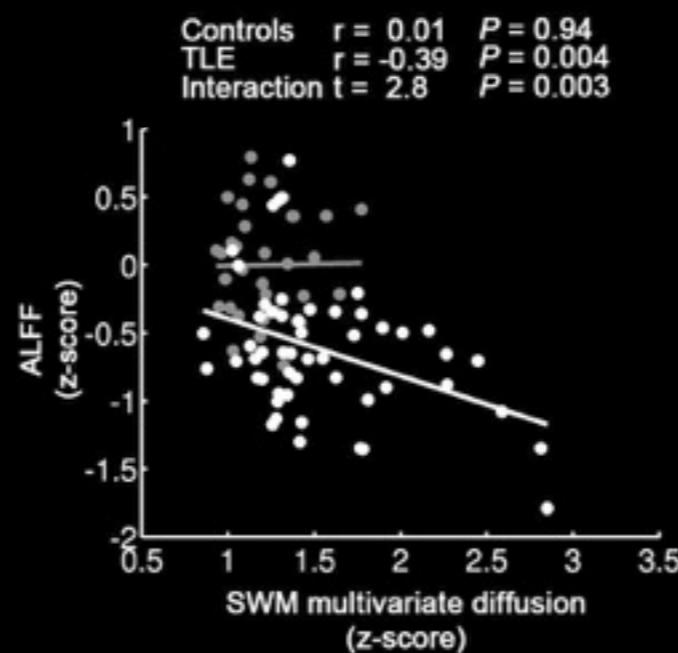
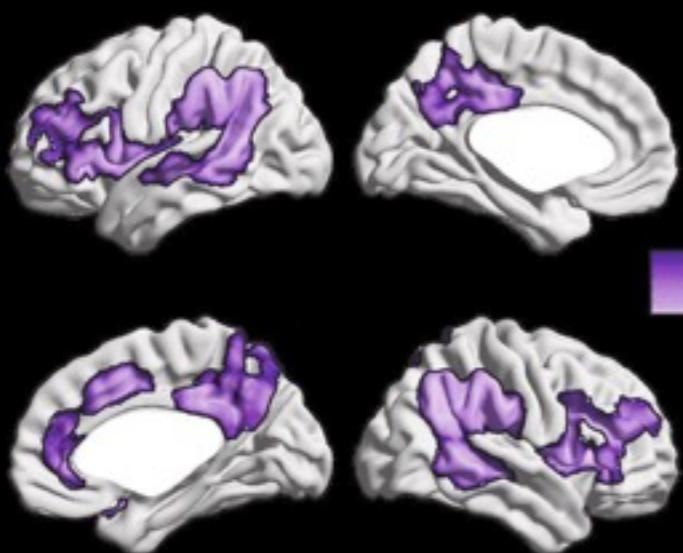
HIPPOCAMPAL ATROPHY → SWM



SWM → FUNCTION



Andrews-Hanna (2012) Neuron



Liu, Bernhardt et al (2016) Brain

INTERIM SUMMARY

FIRST SYSTEMATIC ANALYSIS OF SWM IN TLE

CONVERGENT FA+MD CHANGES REPRODUCIBLE IN LTLE AND RTLE

RELATIVE INDEPENDENCE FROM CORTICAL THINNING

SWM ALTERATIONS MAY LINK
HIPPOCAMPAL PATHOLOGY
TO DMN ANOMALIES

TLE PATHOCONNECTOMICS ARE MODULATED BY
MICROSTRUCTURAL VARIATIONS IN HIPPOCAMPAL PATHOLOGY

Bernhardt, Hong, Liu, Gu, Bassett, Bernasconi, Bernasconi



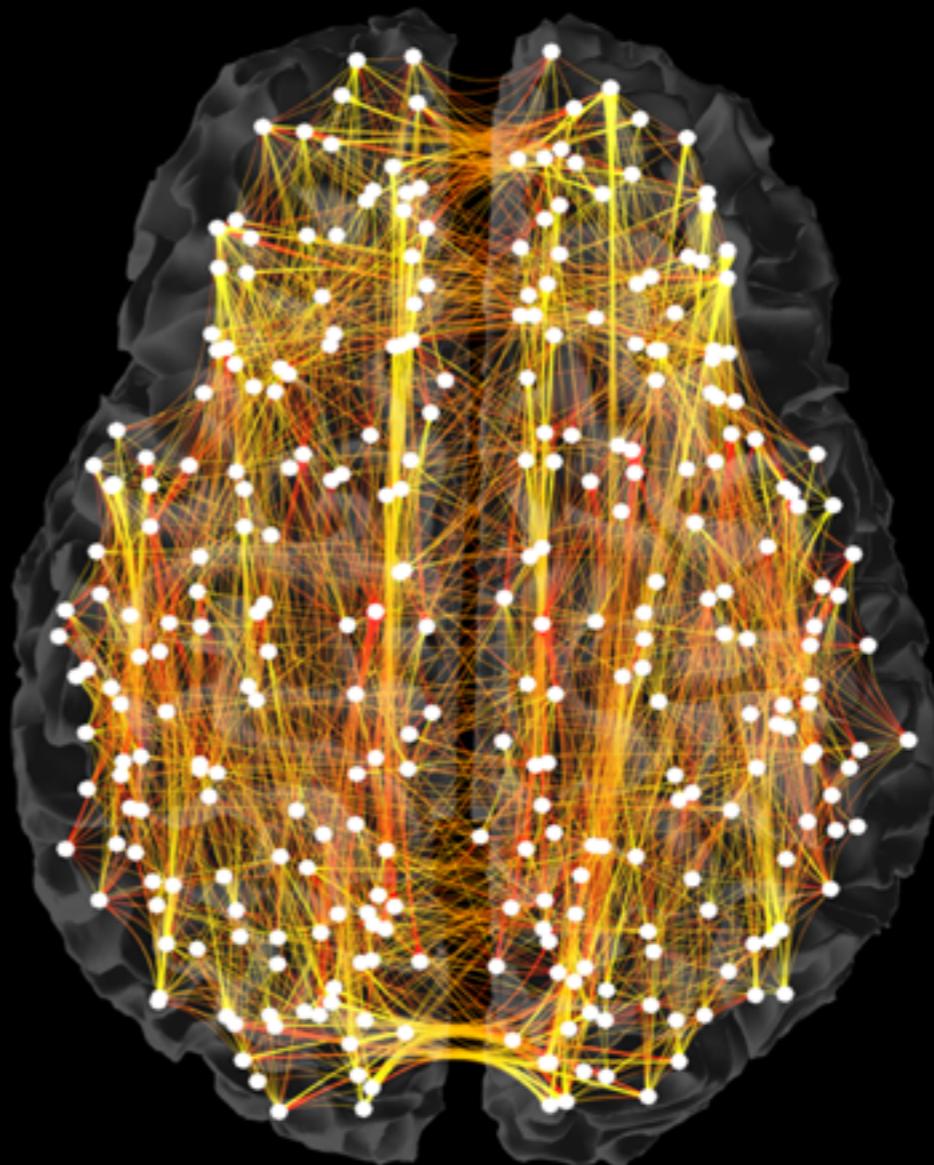
CONNECTOME ANOMALIES

CONNECTOME ASSESSMENTS PROBE
WHOLE BRAIN ORGANIZATION

MAY PROVIDE AN IMPORTANT LINK
TO FUNCTIONAL DYNAMICS

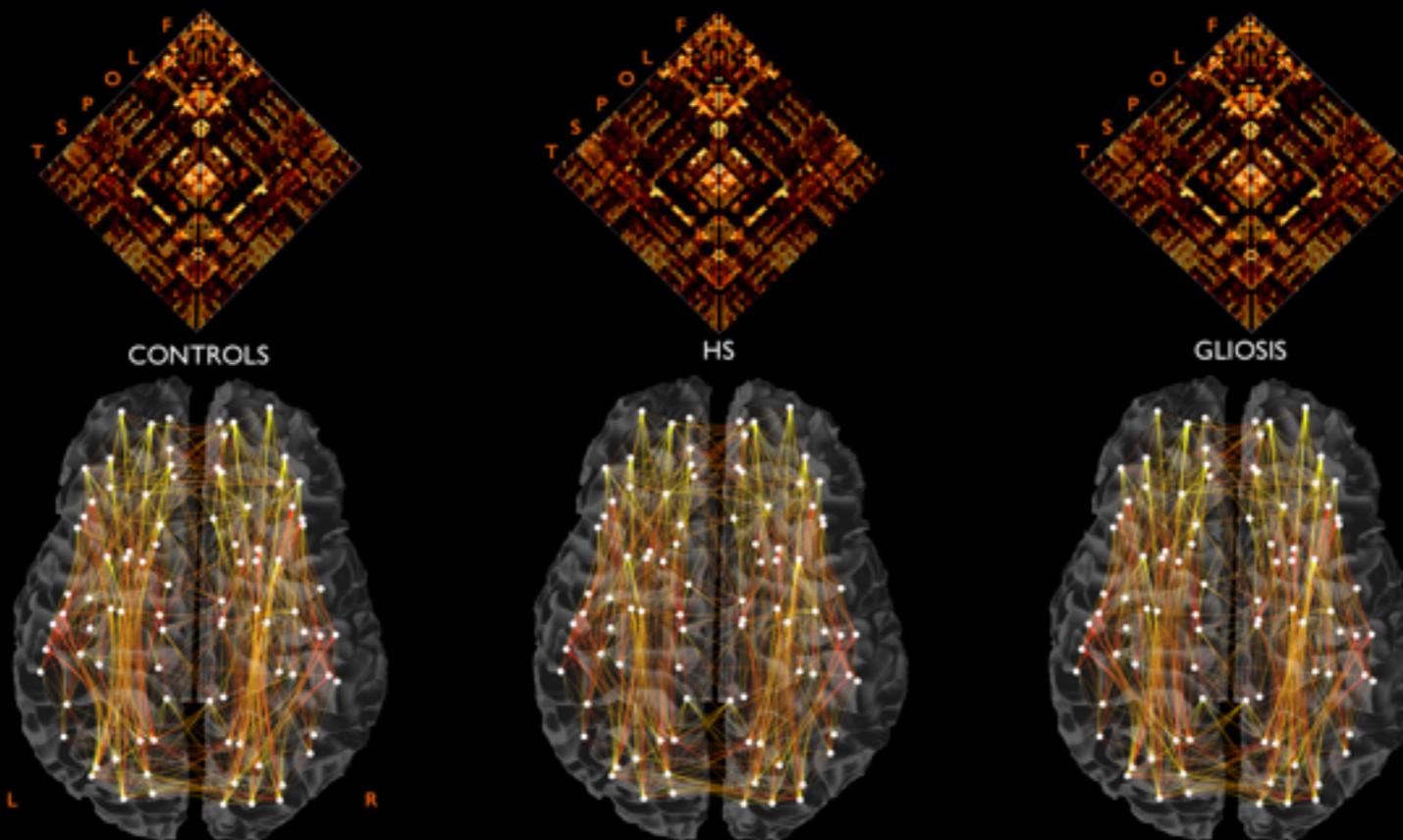
PREVIOUS FINDINGS SUPPORT
NOTION OF TLE AS NETWORK DISORDER

RELATION TO PATHOLOGY IN
MTL EPICENTER NOT CLARIFIED

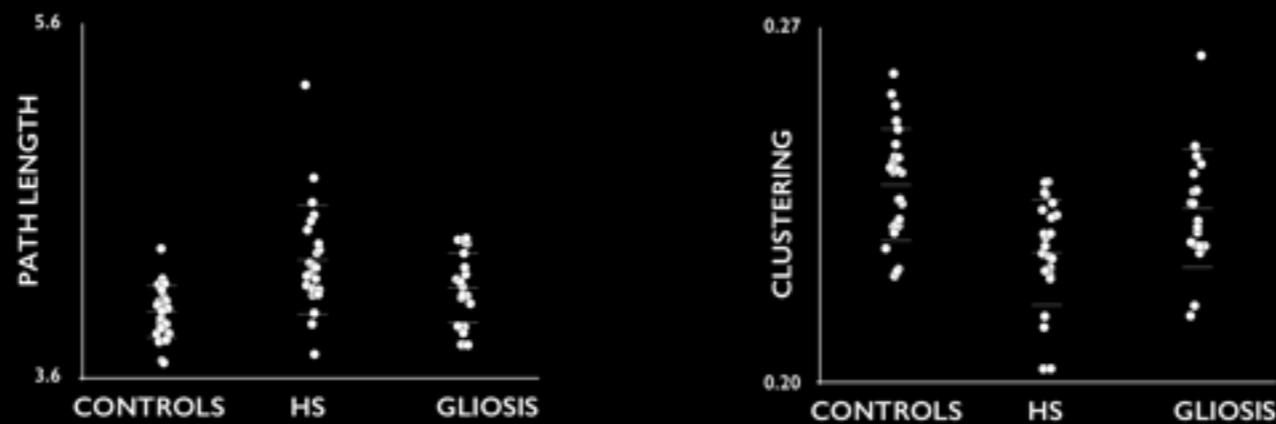


NETWORK TOPOLOGY

CONNECTOMES

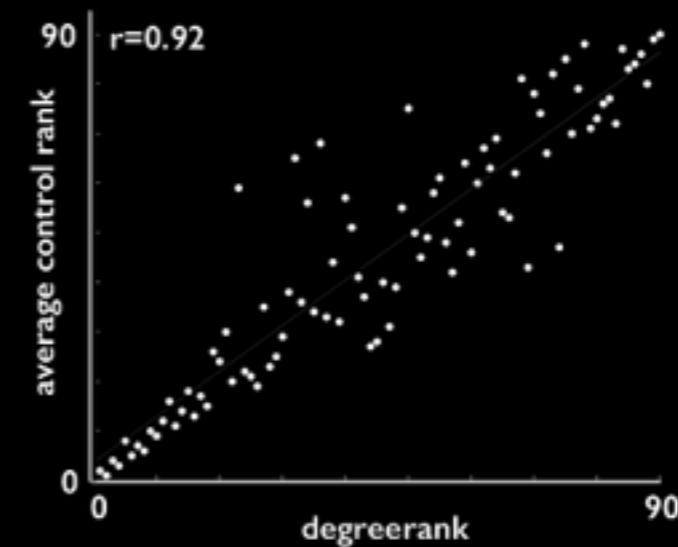
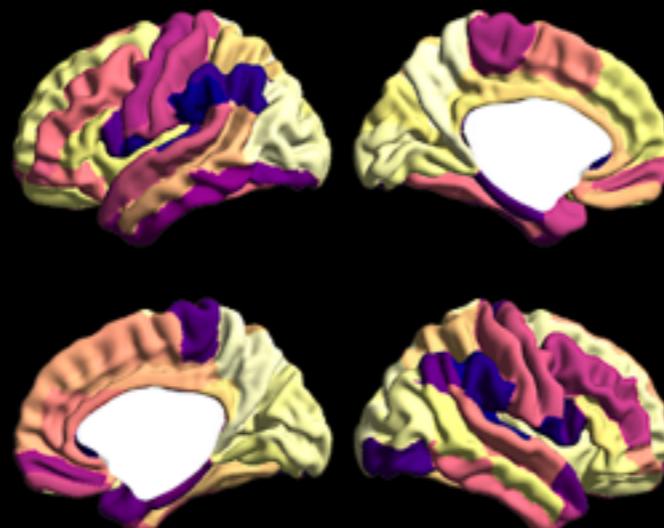


TOPOLOGICAL CHANGES

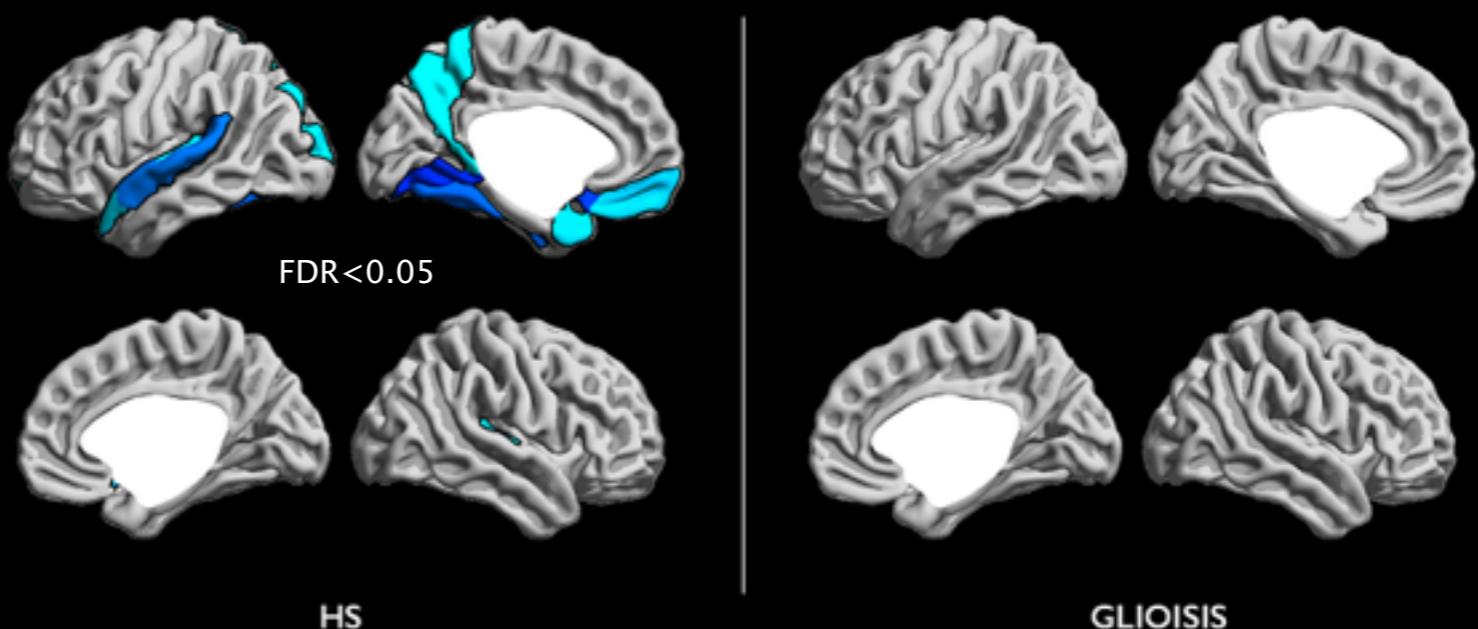
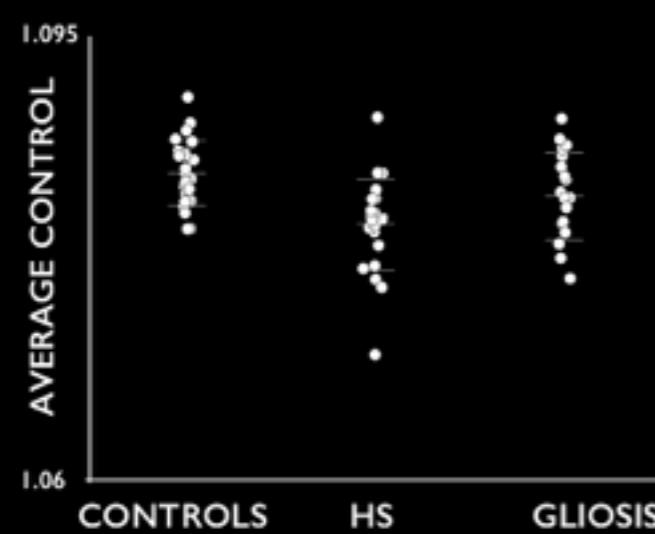


NETWORK CONTROLLABILITY

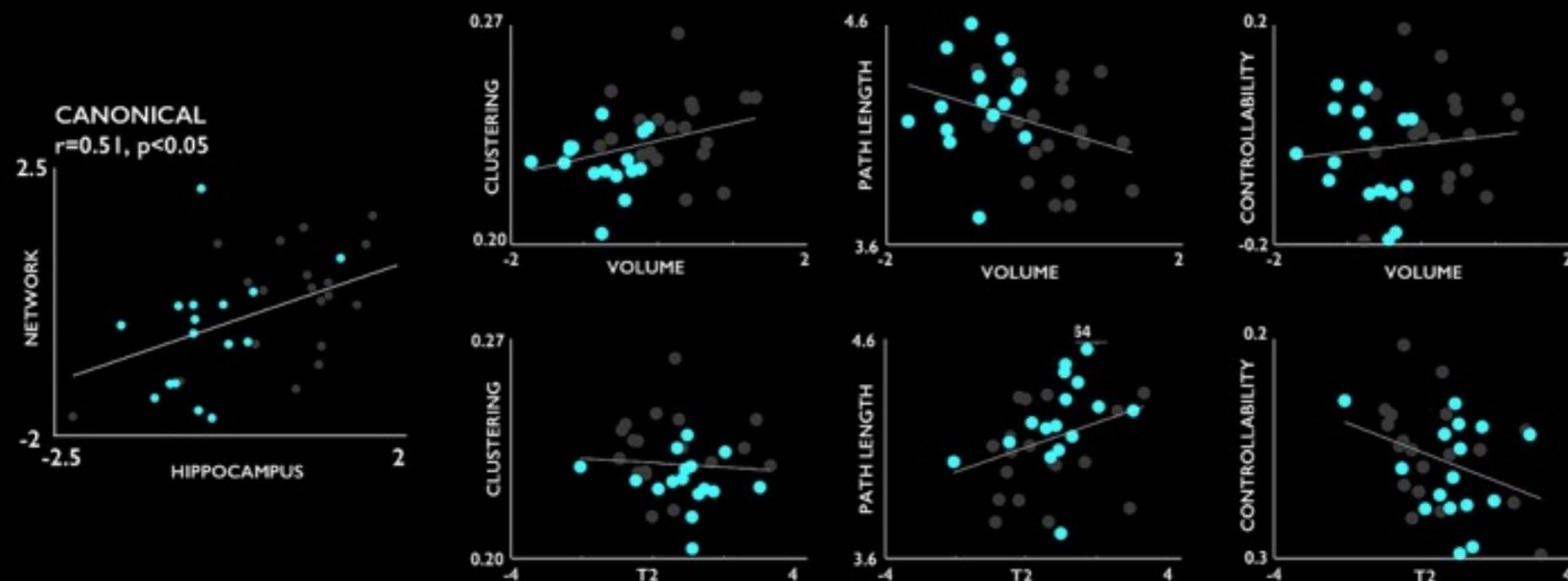
CONTROLLABILITY IN CONTROLS



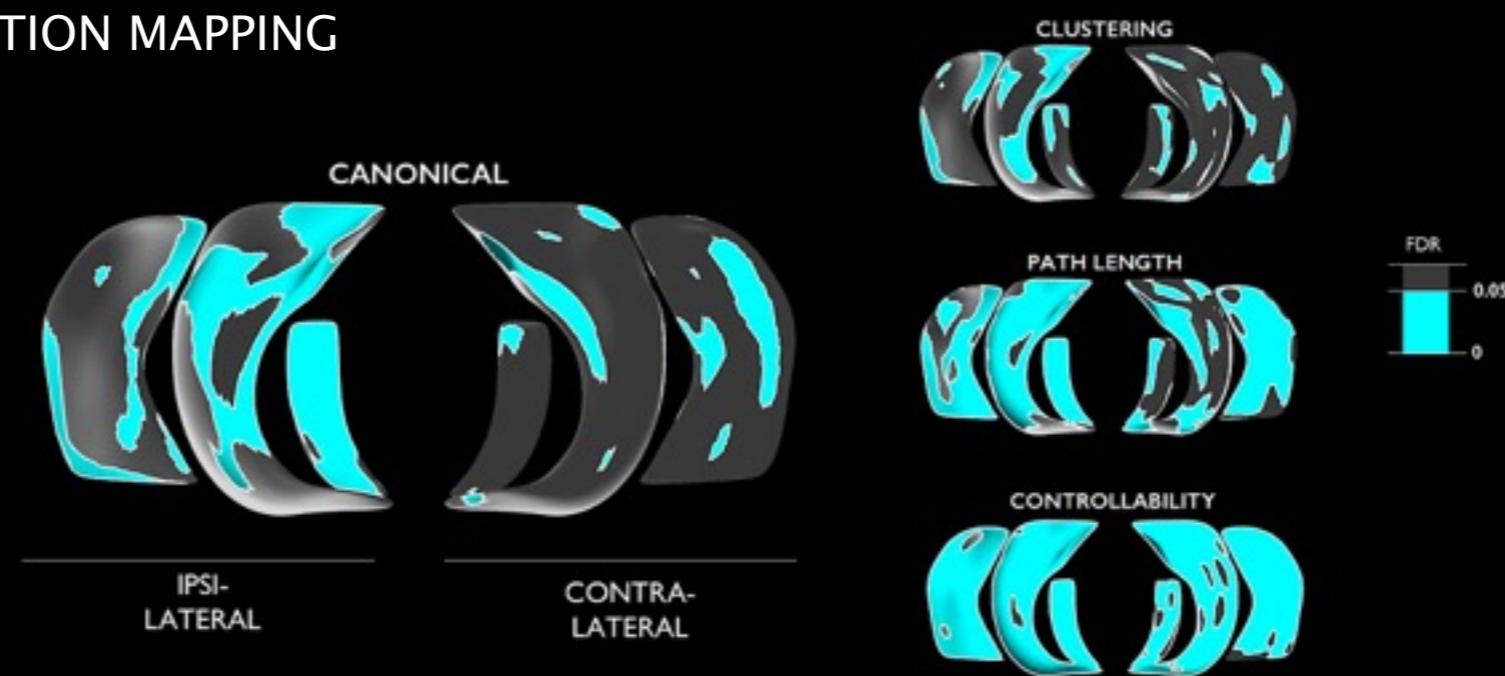
CONTROLLABILITY REDUCTIONS IN TLE-HS



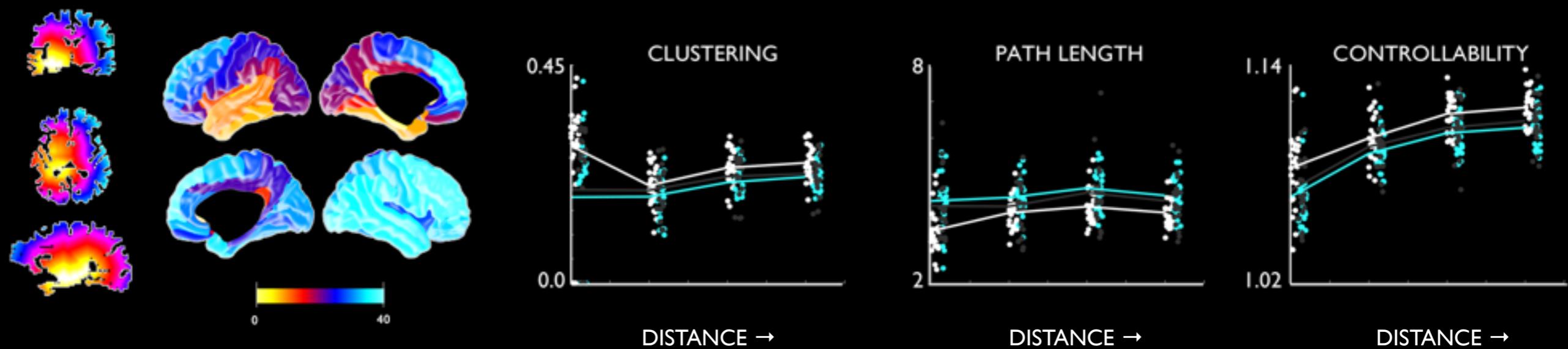
RELATION TO HIPPOCAMPAL FEATURES



BACK PROJECTION MAPPING



DISTANCE-BASED CONNECTOMICS



SUMMARY

DIFFUSION BASED PROFILING OF
WHITE MATTER SYSTEMS:

1)
PROFILING OF DEEP WM TRACTs

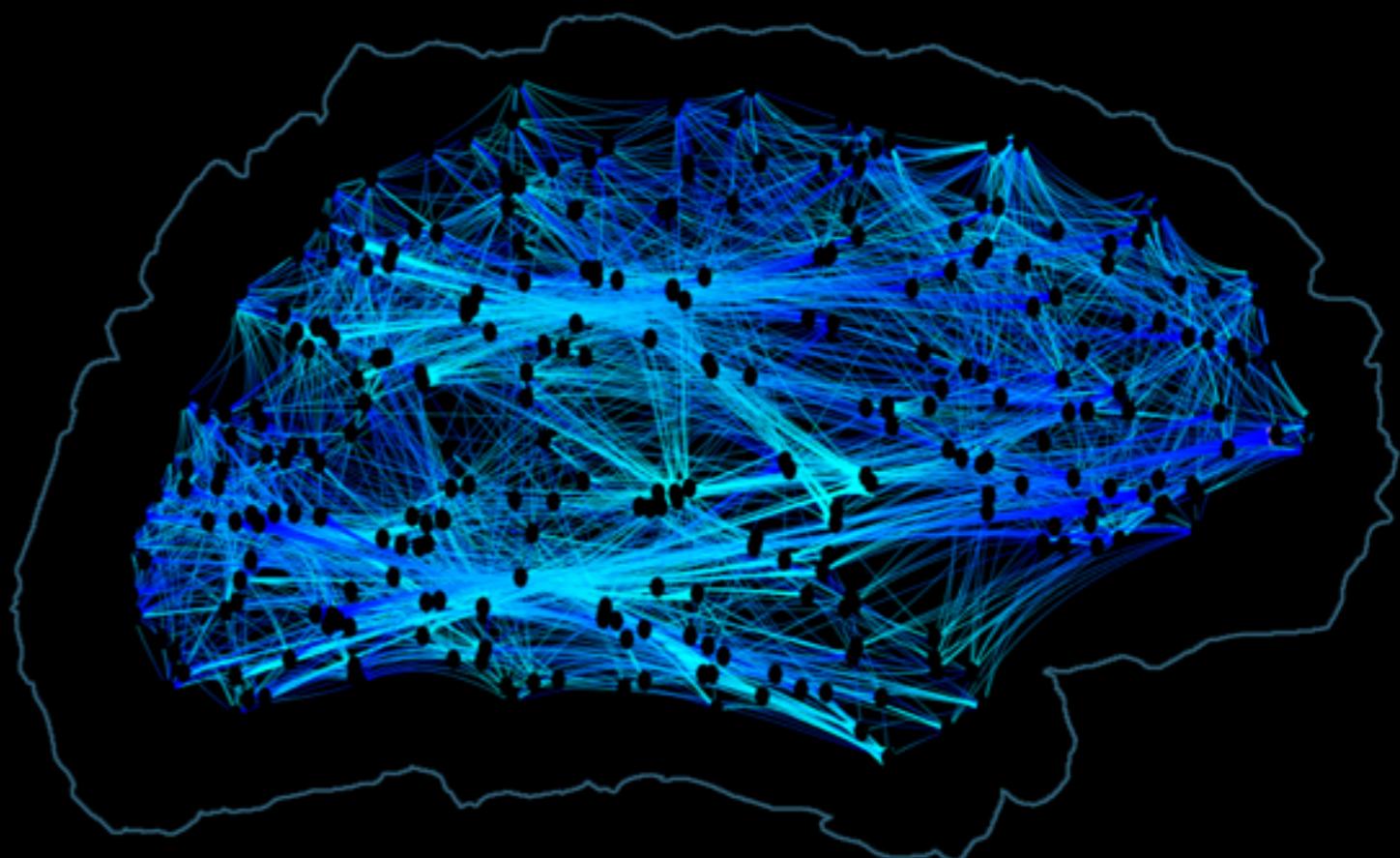
2)
ANALYSIS OF SUPERFICIAL WM

3)
CONNECTOMICS

CONVERGENT FINDINGS SUGGEST
STRONG LINK BETWEEN WM ANOMALIES
AND MESIOTEMPORAL PATHOLOGY

POTENTIAL CASCADING EFFECT
FROM CELL LOSS
TO LARGE-SCALE WHITE MATTER SYSTEMS

ULTIMATELY TRAINING THE FUNCTIONAL
REPERTOIRE, PARTICULARLY IN DMN



Neuroimaging of Epilepsy Lab

MICA Lab

Sofie Valk

Seok-Jun Hong

Brian Hyung

Tabea Haas Heger

Neda Bernasconi

Andrea Bernasconi

Jessie Kulaga Yoskovitz

Seok-Jun Hong

Benoit Caldairou

Min Liu

Sophie Adler

Francesco Deleo

Epilepsy Group at MNI

Jeffrey Hall

Marie Christine Guiot

U Queretaro

Luis Concha



Together We Will.

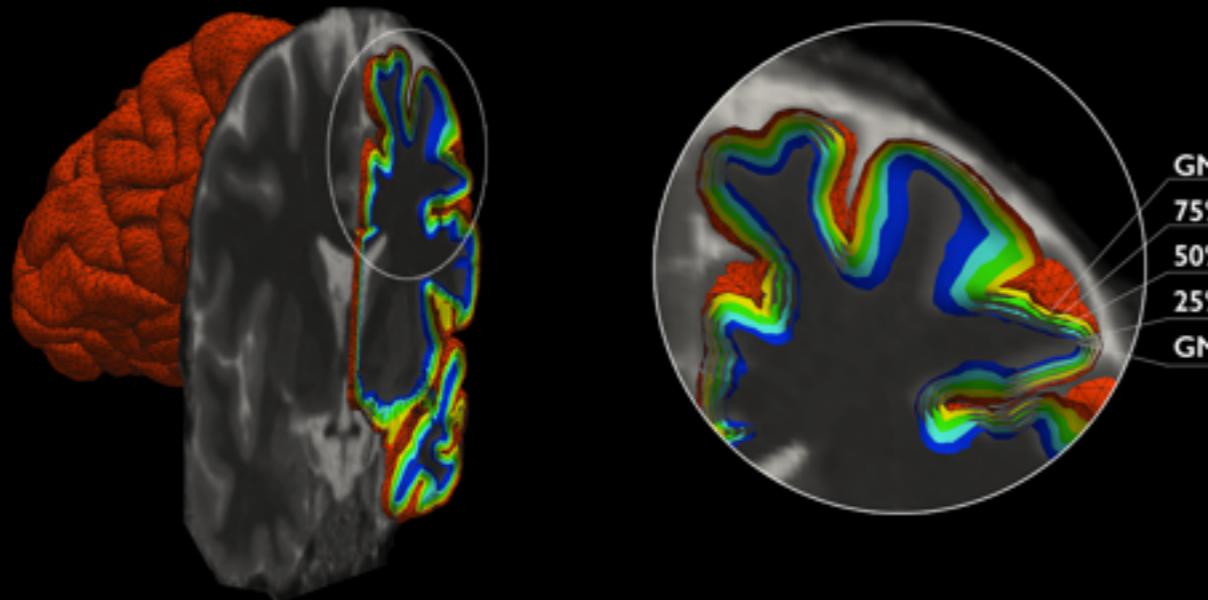


SOCIETY

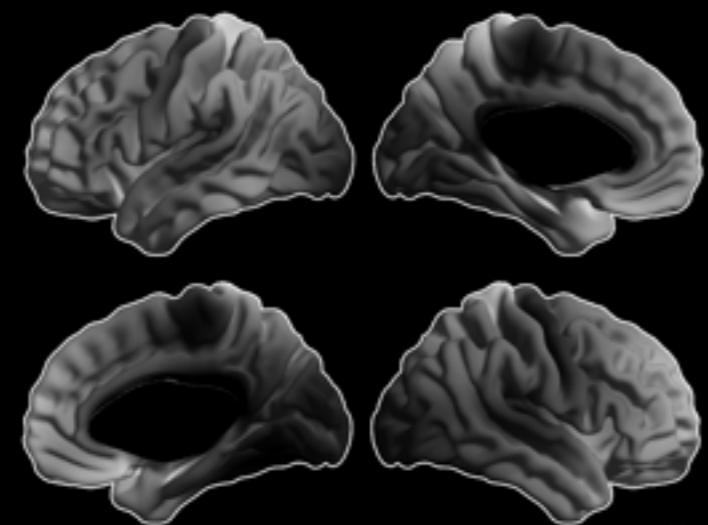


Canadian League Against Epilepsy
Sous le signe de l'espérance contre l'épilepsie

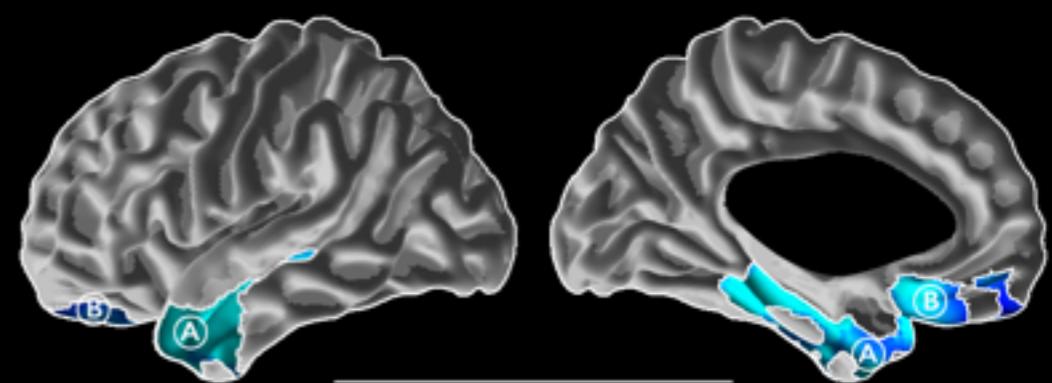
POTENTIAL CO-LOCALIZATION WITH MYELIN CHANGES



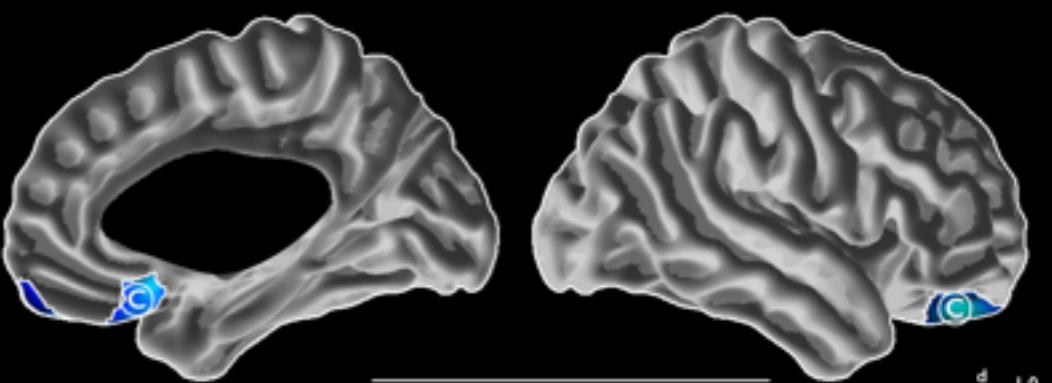
SURFACE-BASED FEATURE SAMPLING



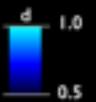
MEAN qT_1 IN HEALTHY CONTROLS



IPSILATERAL



CONTRALATERAL



CO-LOCALIZATION WITH FOLDING CHANGES

