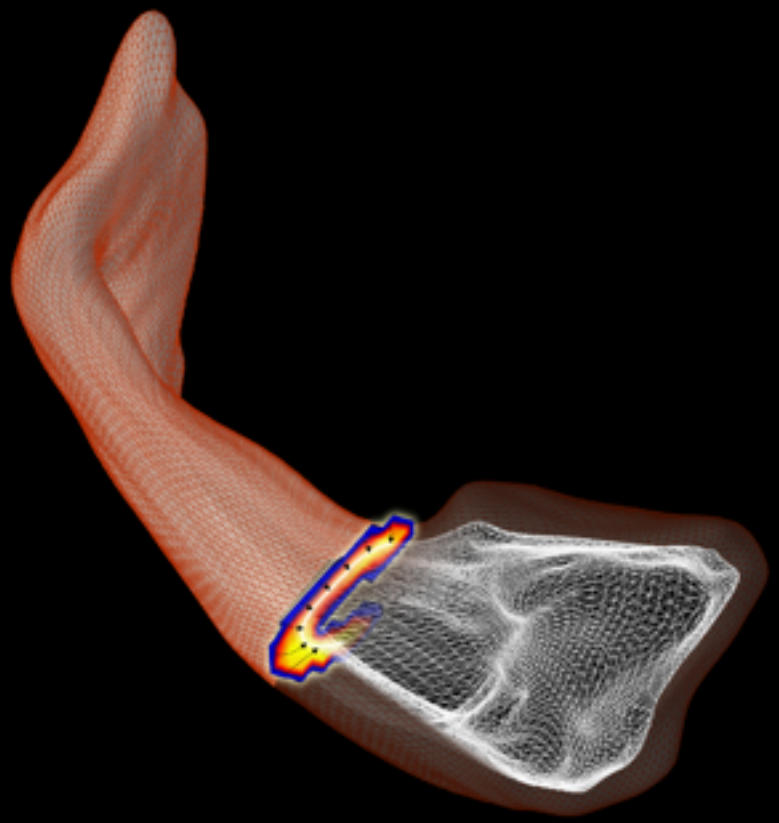


MULTIMODAL IMAGING IN DRUG-RESISTANT EPILEPSY

FROM HIPPOCAMPAL SUBFIELDS TO LARGE-SCALE NETWORKS

Boris Bernhardt, PhD

http://mica-mni.github.io

EPILEPSY

PREVALENT CHRONIC
NEUROLOGICAL DISORDER

CHARACTERIZED BY SEIZURES

30% OF PATIENTS ARE
DRUG-RESISTANT

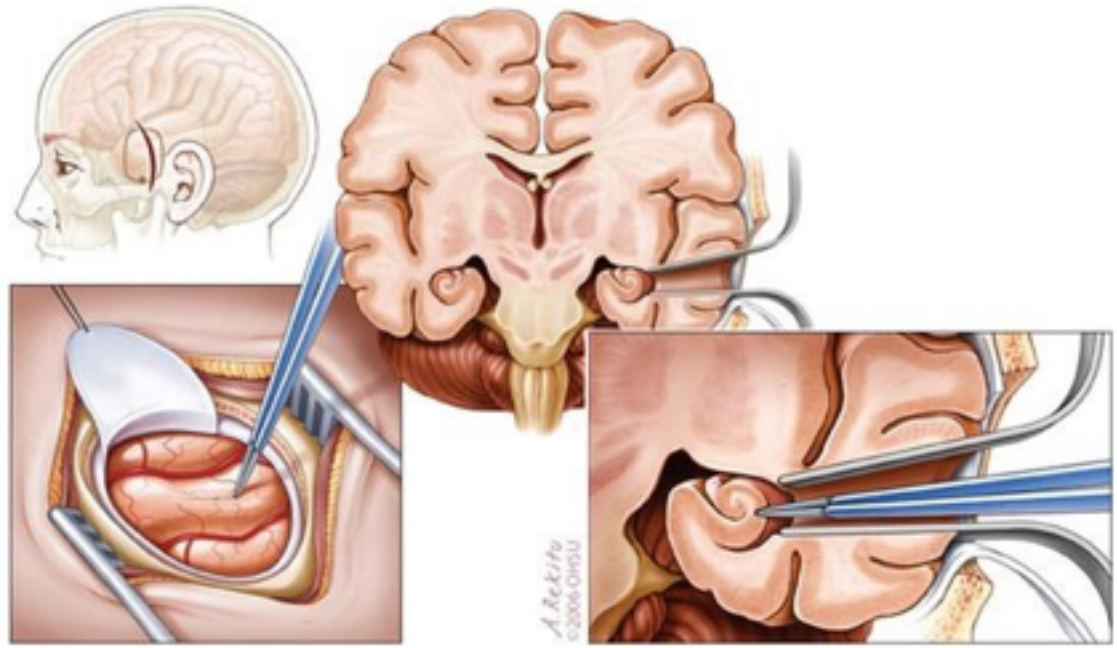
HIGH RISKS OF
MORBIDITY, MORTALITY, AND
PSYCHOSOCIAL DEPRIVATION

TEMPORAL LOBE EPILEPSY

MOST COMMON DRUG-RESISTANT EPILEPSY IN ADULTS

SEIZURES ARISING FROM TL

SURGERY MOST EFFECTIVE TREATMENT [Wiebe et al. (2001) NEJM]

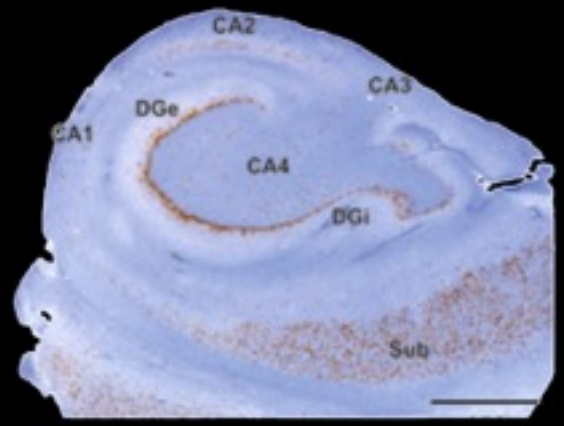


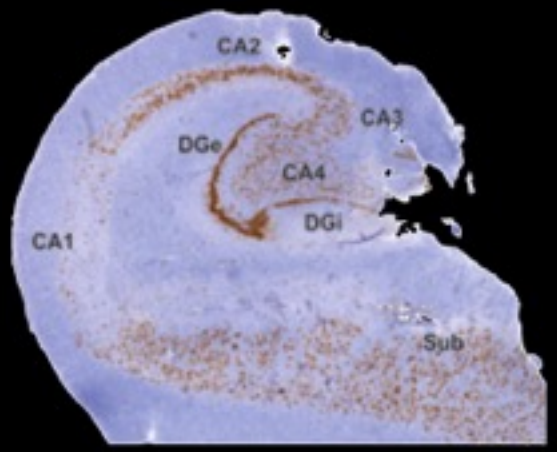
Spencer & Burchiel (2012) Epilepsy Research and Treatment

TEMPORAL LOBE EPILEPSY

Pathological hallmark: hippocampal sclerosis (HS) – not a single entity

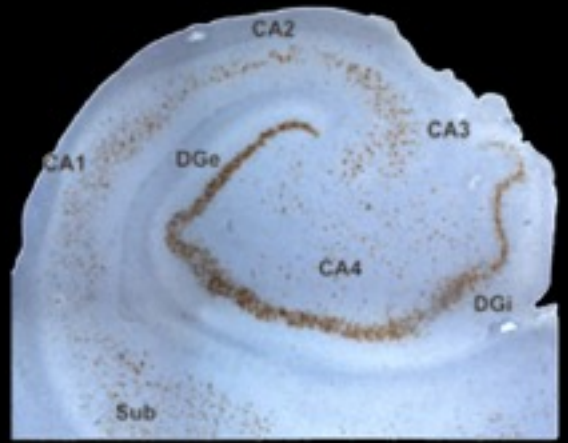
CA1+CA4 cell loss + gliosis

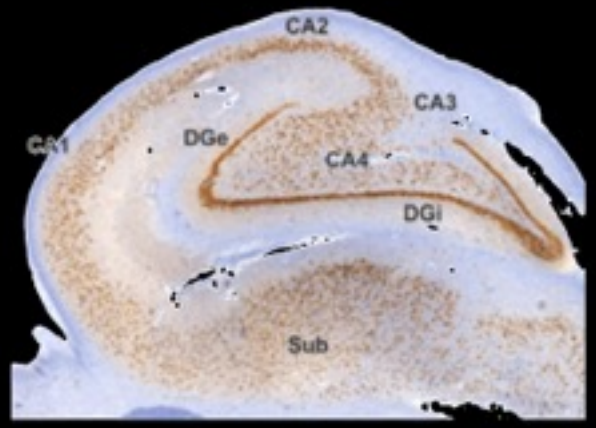




CA1 cell loss + gliosis

CA4 cell loss + gliosis





gliosis only

Blümcke et al (2013) Epilepsia

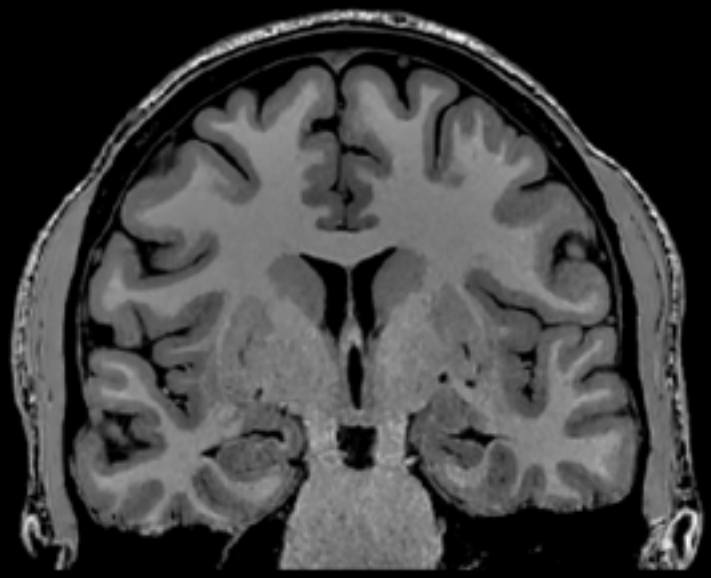
HIPPOCAMPAL PATHOLOGY AND IMAGING IN TLE

MRI plays key role in detecting HS non-invasively

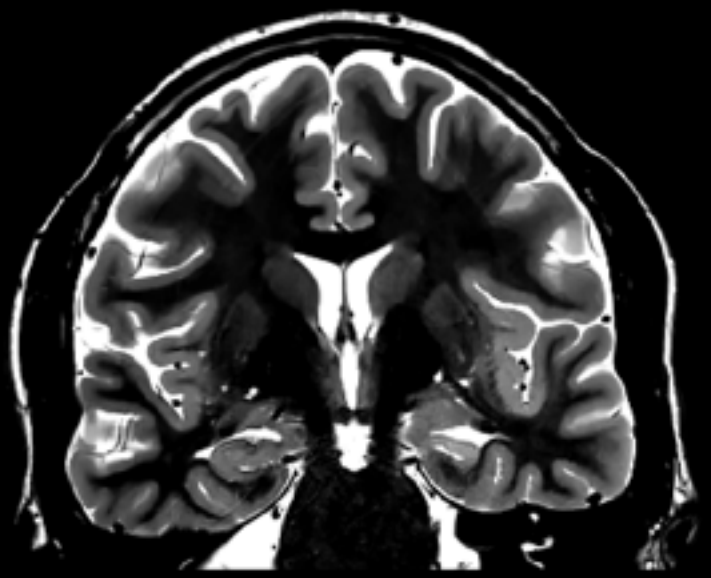
Atrophy and T2w increases can lateralize seizure focus in patients with HS

In the clinics: most frequently done visually

Increasing proportions of patients with less remarkable anomalies

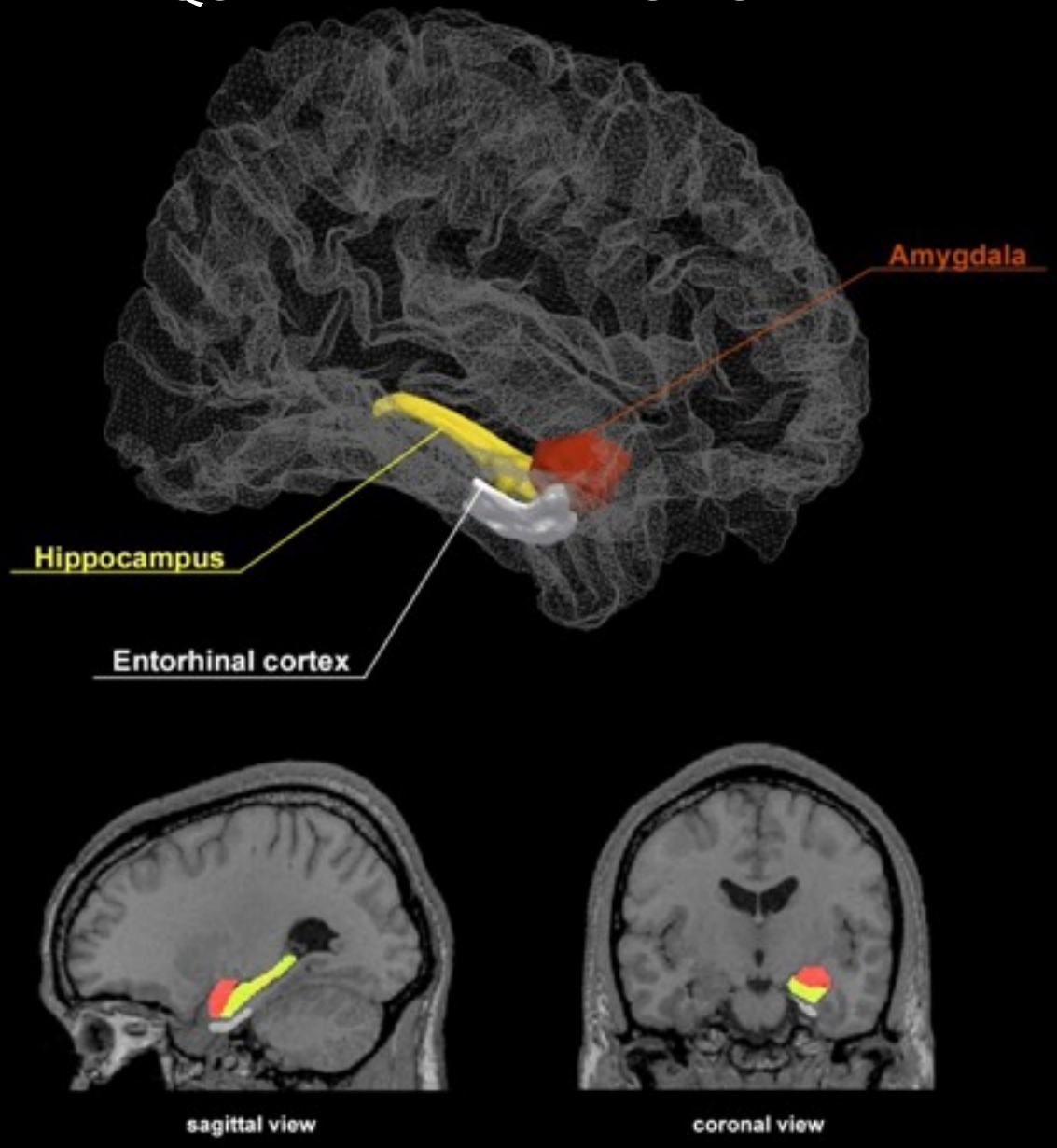


T1-weighted



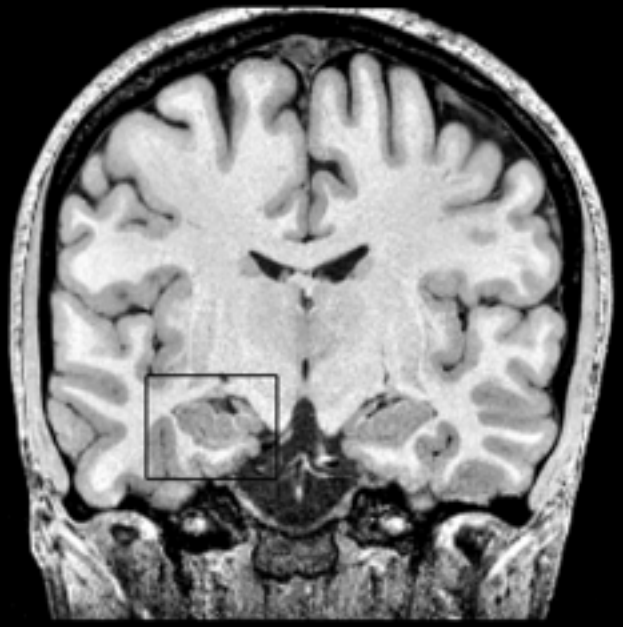
T2-weighted

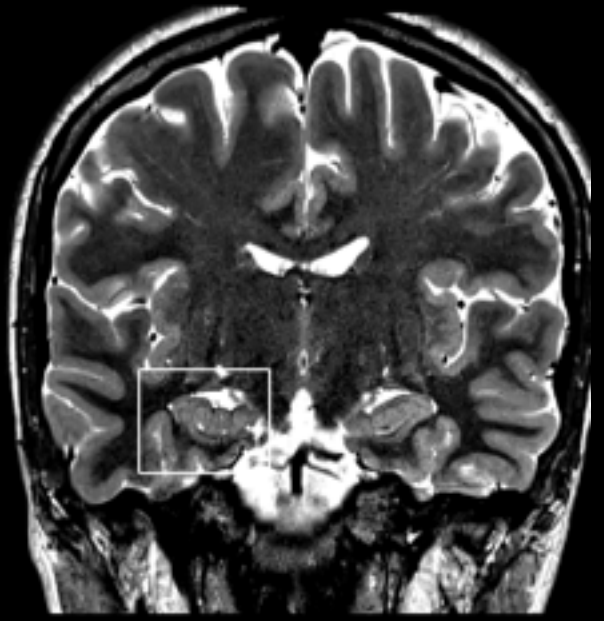
QUANTITATIVE IMAGING IN TLE



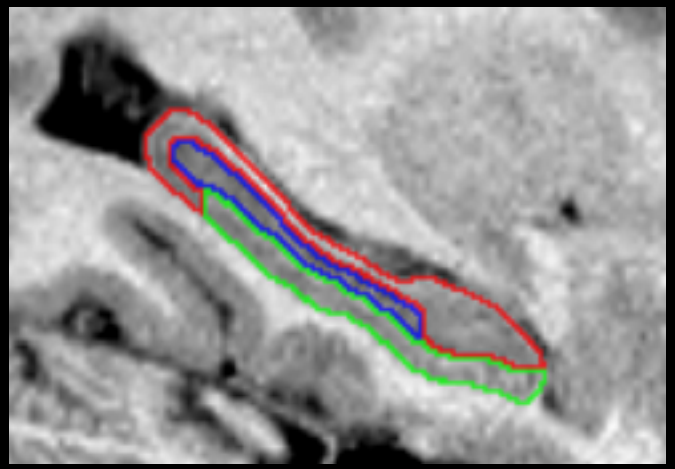
Cascino et al (1991) Annals of Neurology, Jackson et al (1995) Neurology

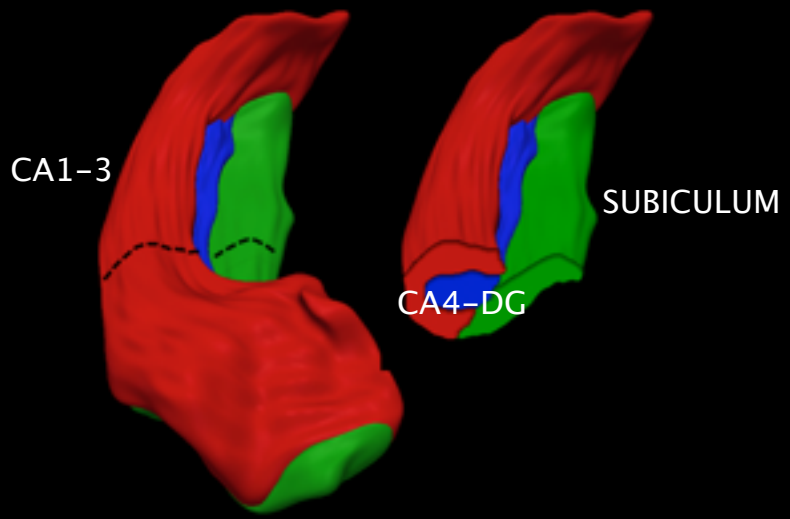
Kuzniecky et al (1999) Neurology, Bernasconi et al (2003) Brain





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





Kulaga -Yoskovitz et al. (2015) Scientific Data

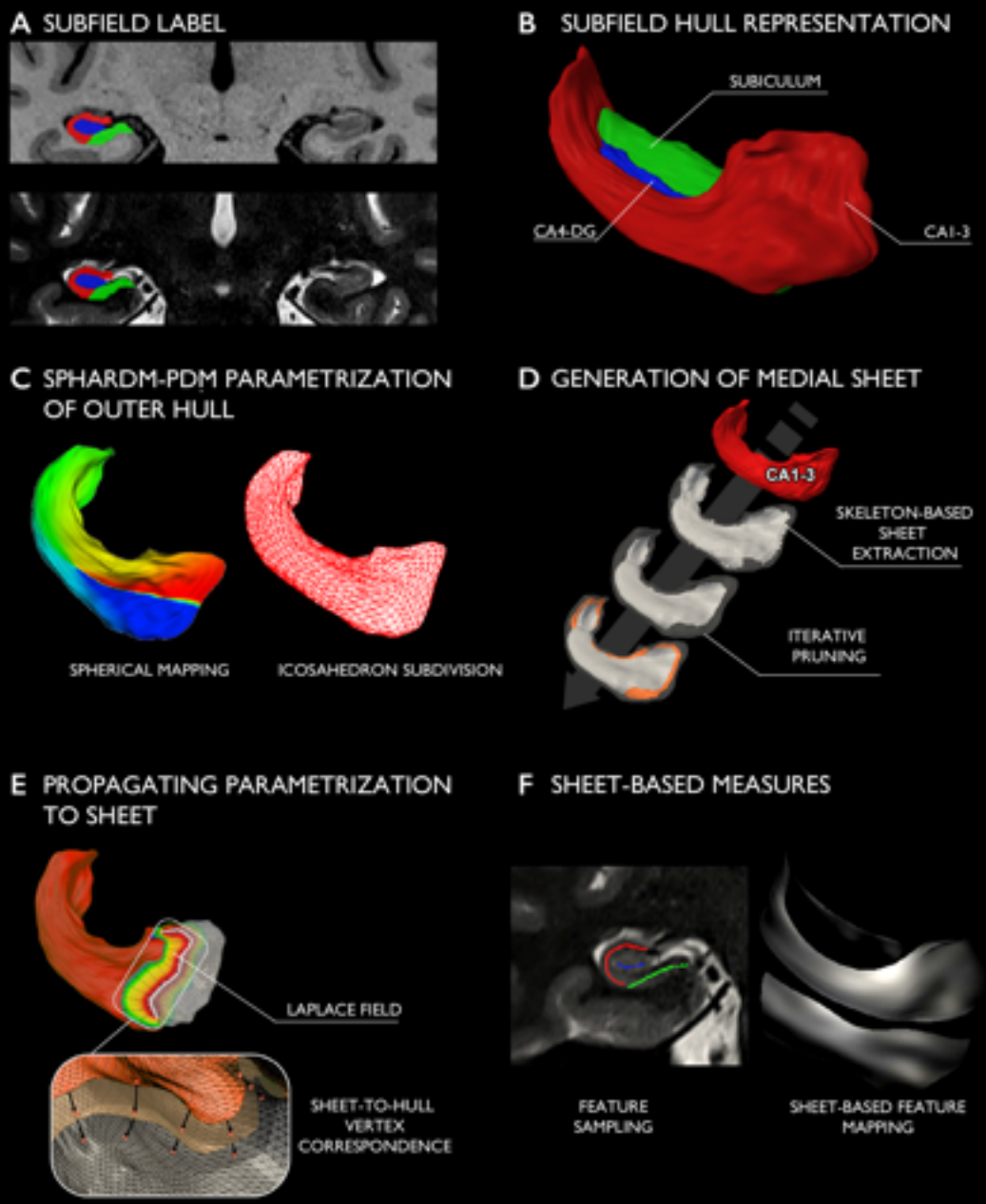
STUDY PURPOSE

IDENTIFY MRI SIGNATURES OF TLE-HS AND TLE-G

DESIGN:

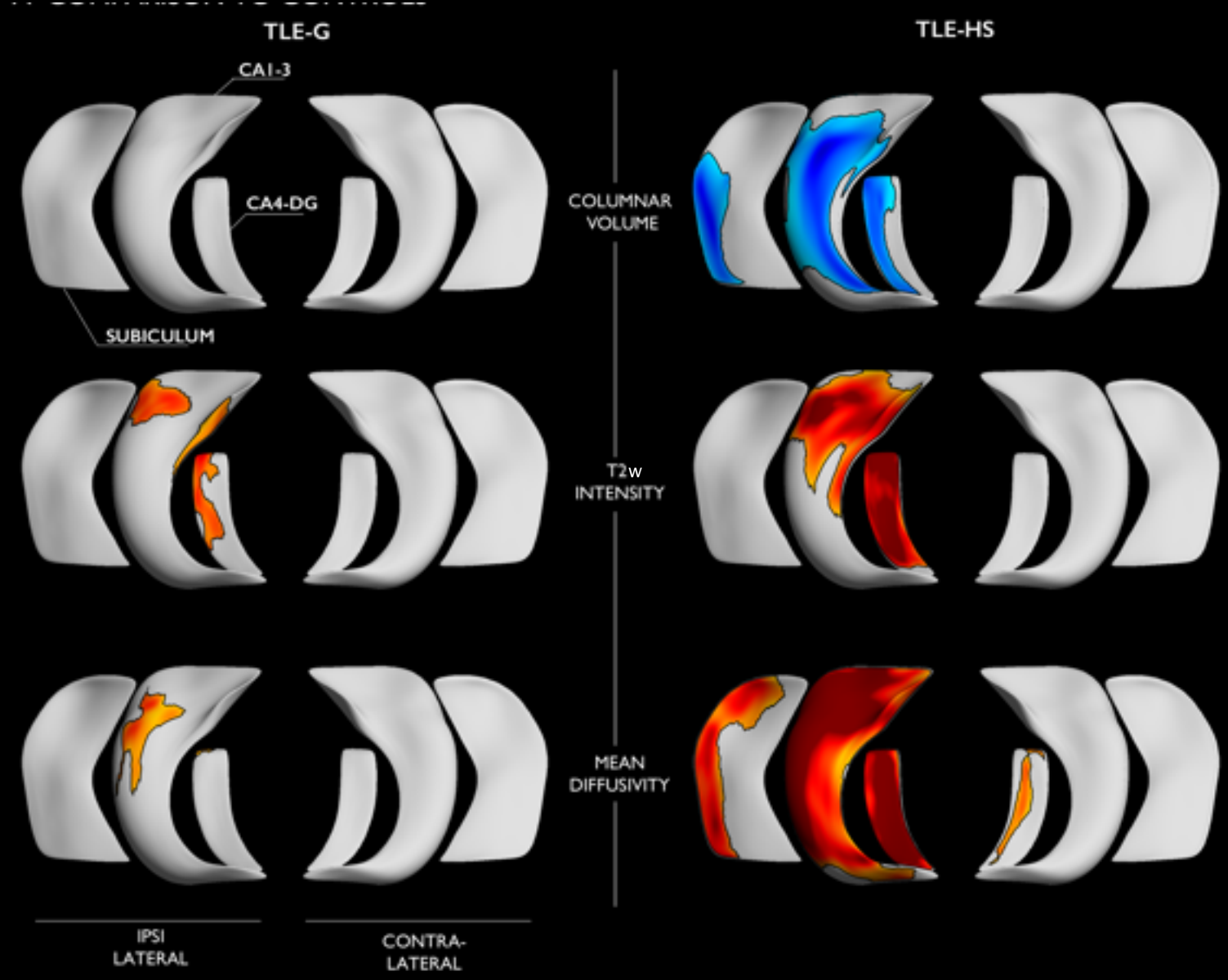
- Consecutive series of 39 unilateral TLE patients who had high resolution preoperative MRI, no mass lesions, surgical treatment, and ILAE HS scoring
  - 20 TLE-HS (10 HS-1, 6 HS-2, 4 HS-3), 19 TLE-G
  - 25 age- and sex-matched controls
- Multi-modal 3T MRI in all, in addition to clinical imaging
  - high-resolution T1w (0.6 mm, 2 averages), T2w (0.4×0.4×2.0 mm)
  - standard DWI and RS-FMRI
- Hippocampal subfield segmentations in all

IMAGE PROCESSING



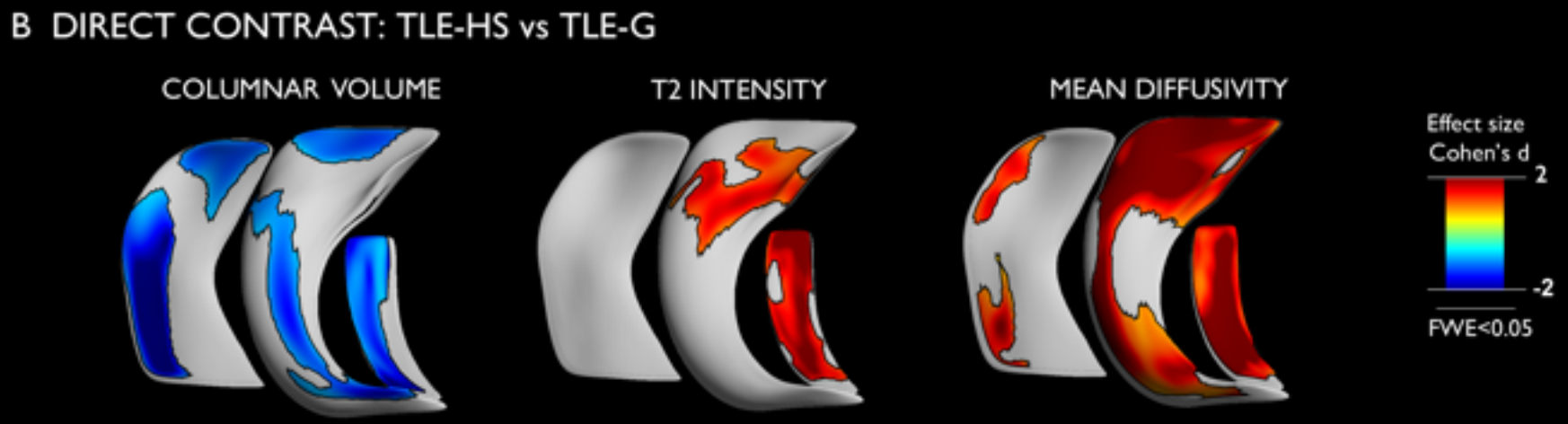
Kim et al (2015) MICCAI

FEATURE-SPECIFIC COMPARISON TO CONTROLS

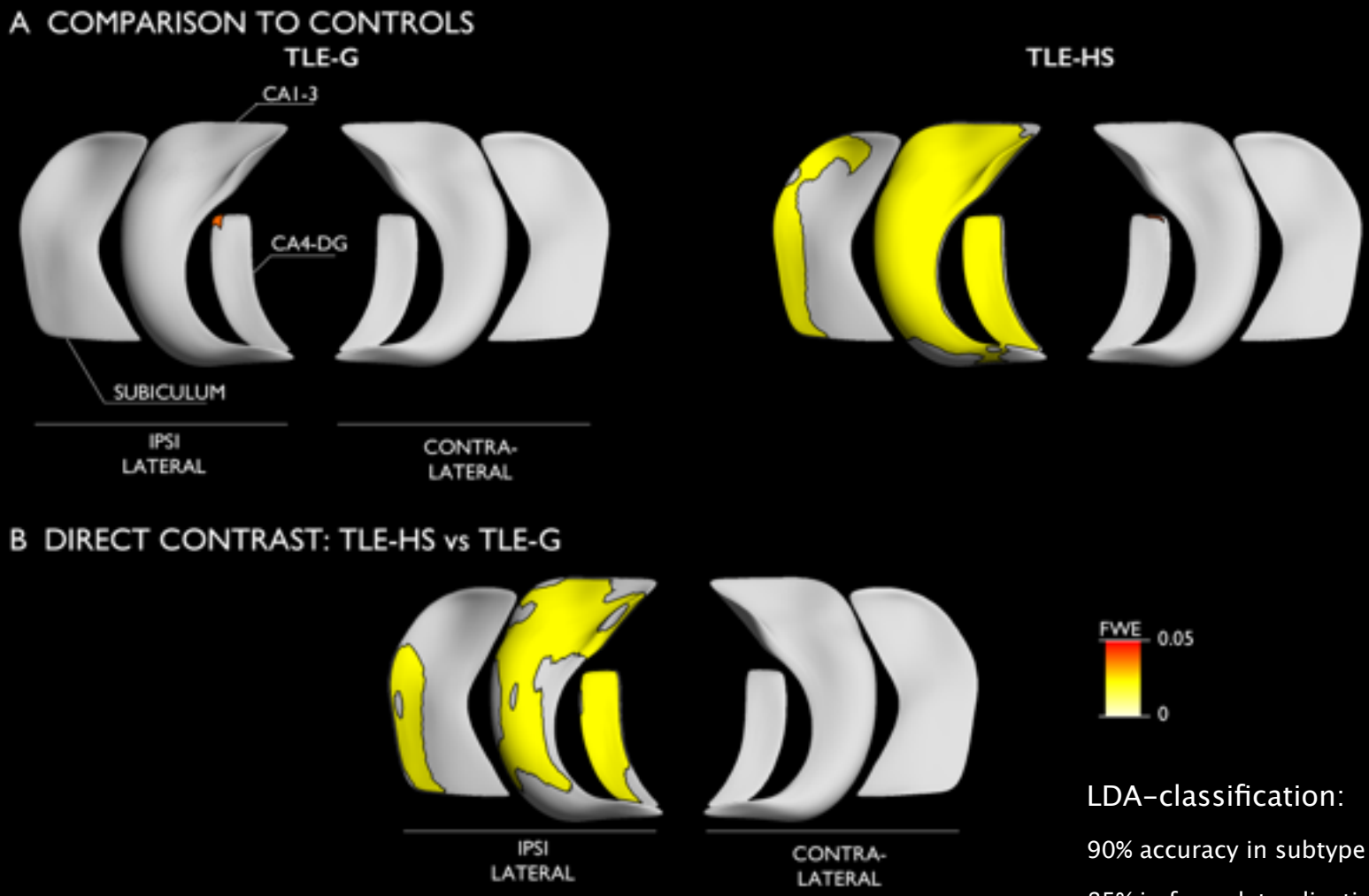


Bernhardt et al (2016) Annals of Neurology

DIRECT CONTRASTS



MULTIVARIATE SYNTHESIS

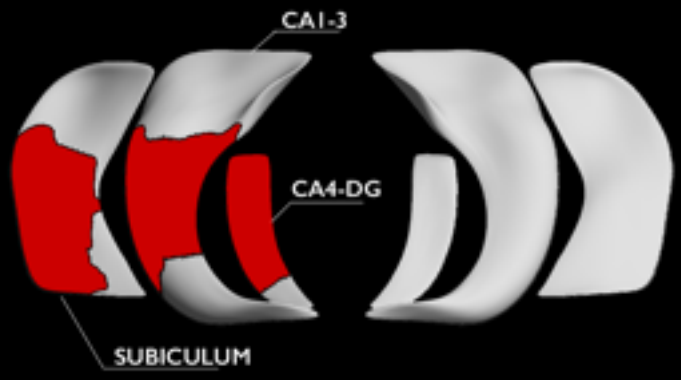


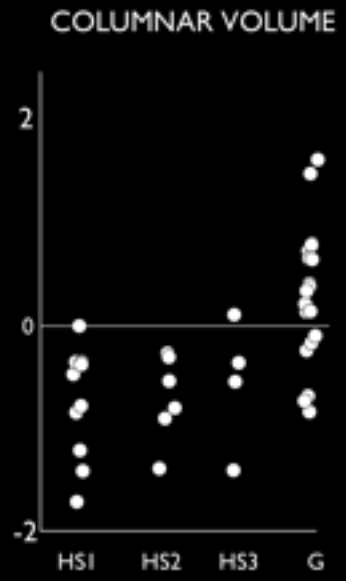
LDA-classification:

90% accuracy in subtype discrimination

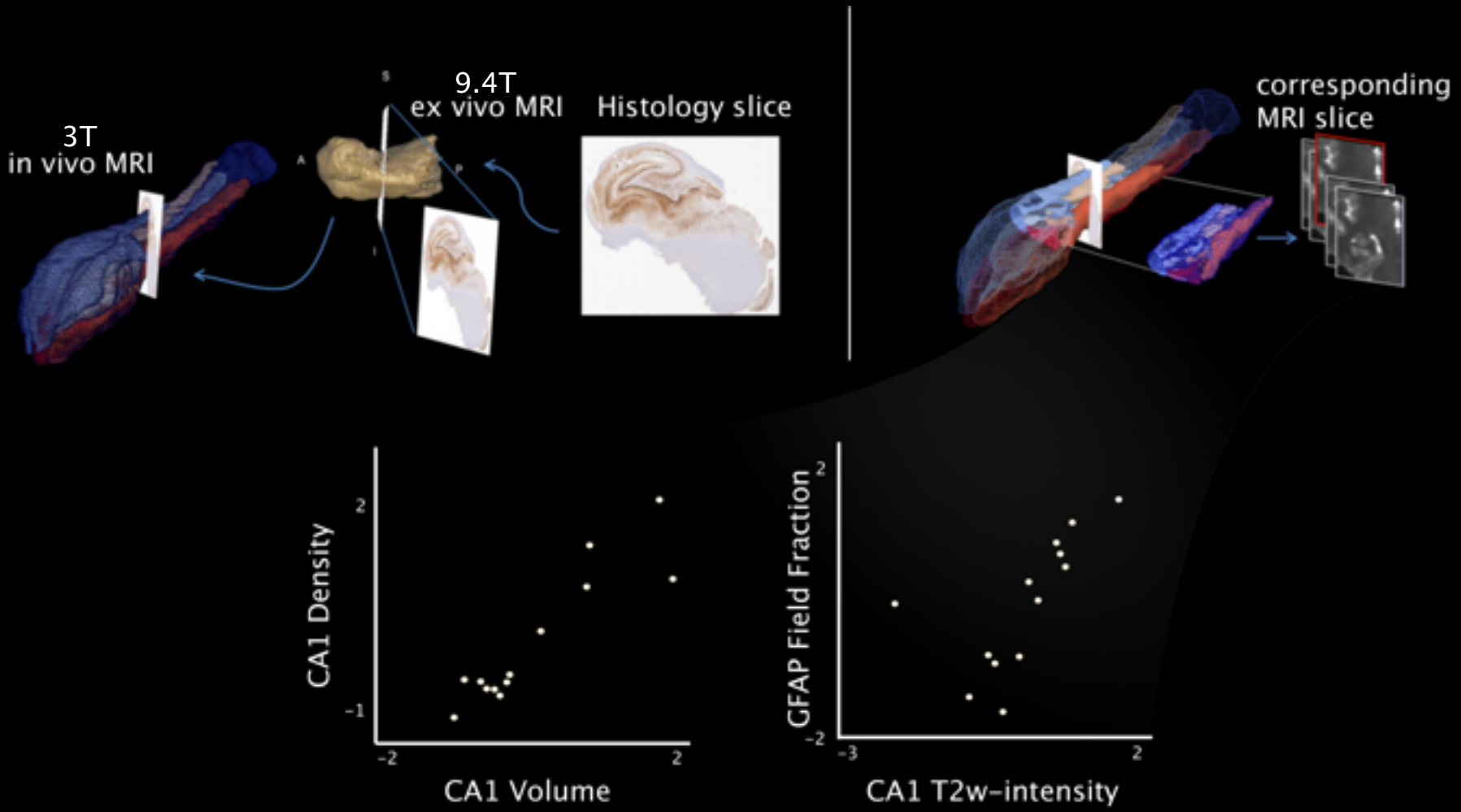
85% in focus lateralization

RELATION TO SPECIFIC HISTOLOGICAL HS GRADES





VALIDATION OF IN VIVO FINDINGS WITH QUANTITATIVE HISTOPATHOLOGY



SUBFIELD-SPECIFIC CORRELATIONS BETWEEN MRI AND HISTOLOGY

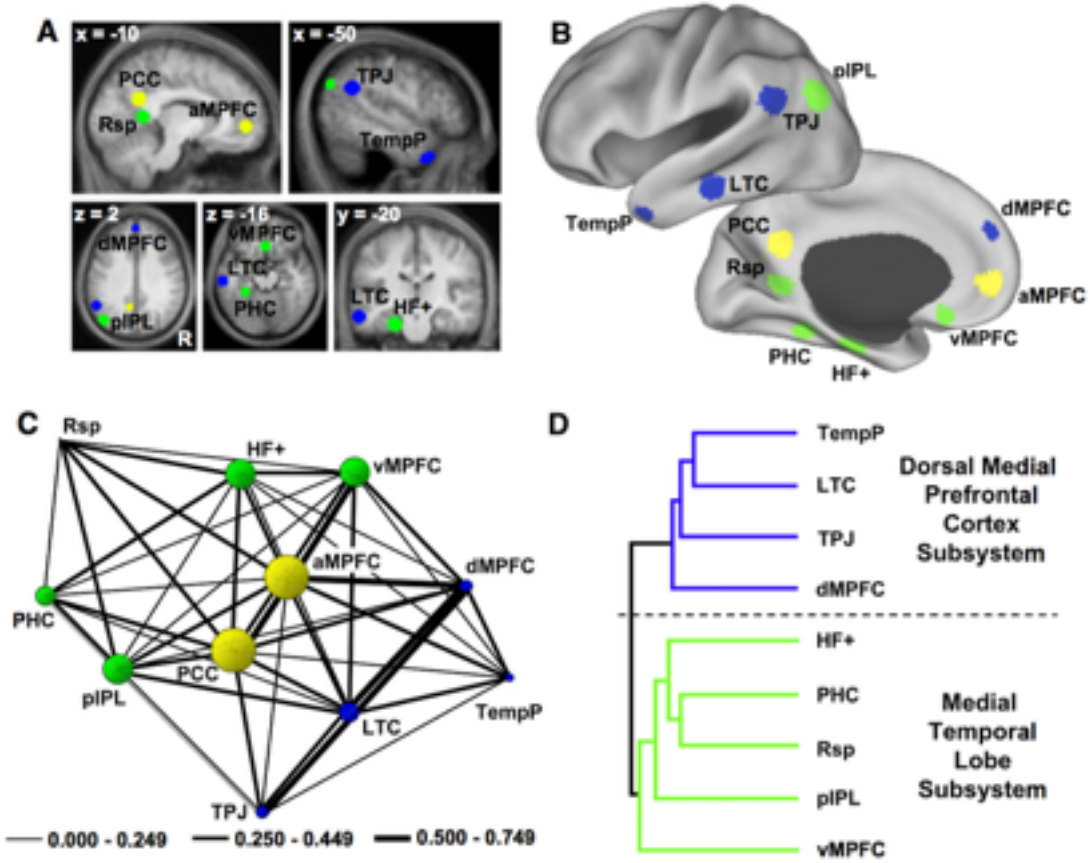
Goubran et al (2016) Hum Brain Mapp

FUNCTION

RESTING-STATE FMRI ANALYSIS
PROVIDE INFORMATION ON
INTRINSIC FUNCTIONAL NETWORKS

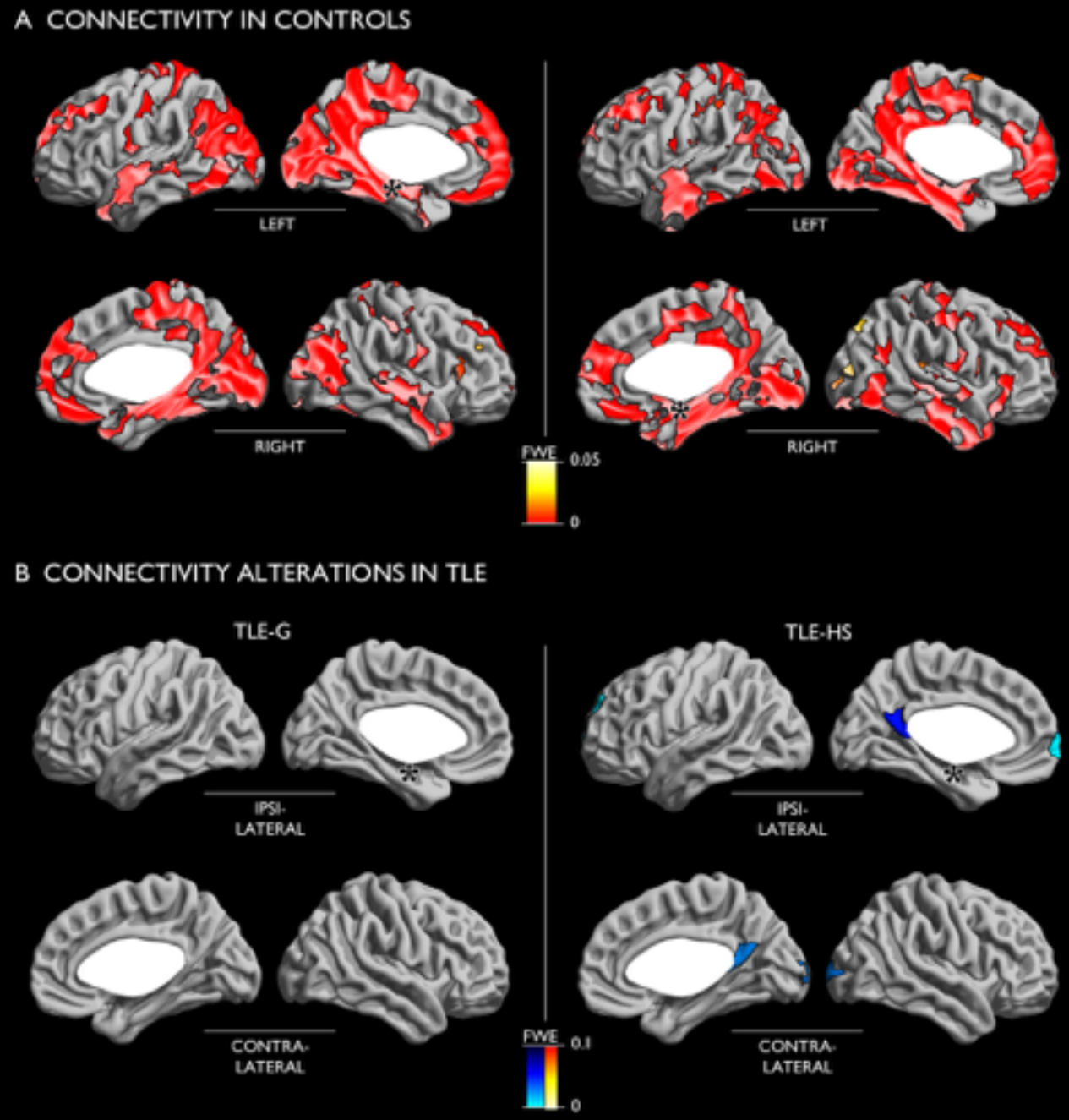
HIPPOCAMPUS HIGHLY INTEGRATED
WITH DMN

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

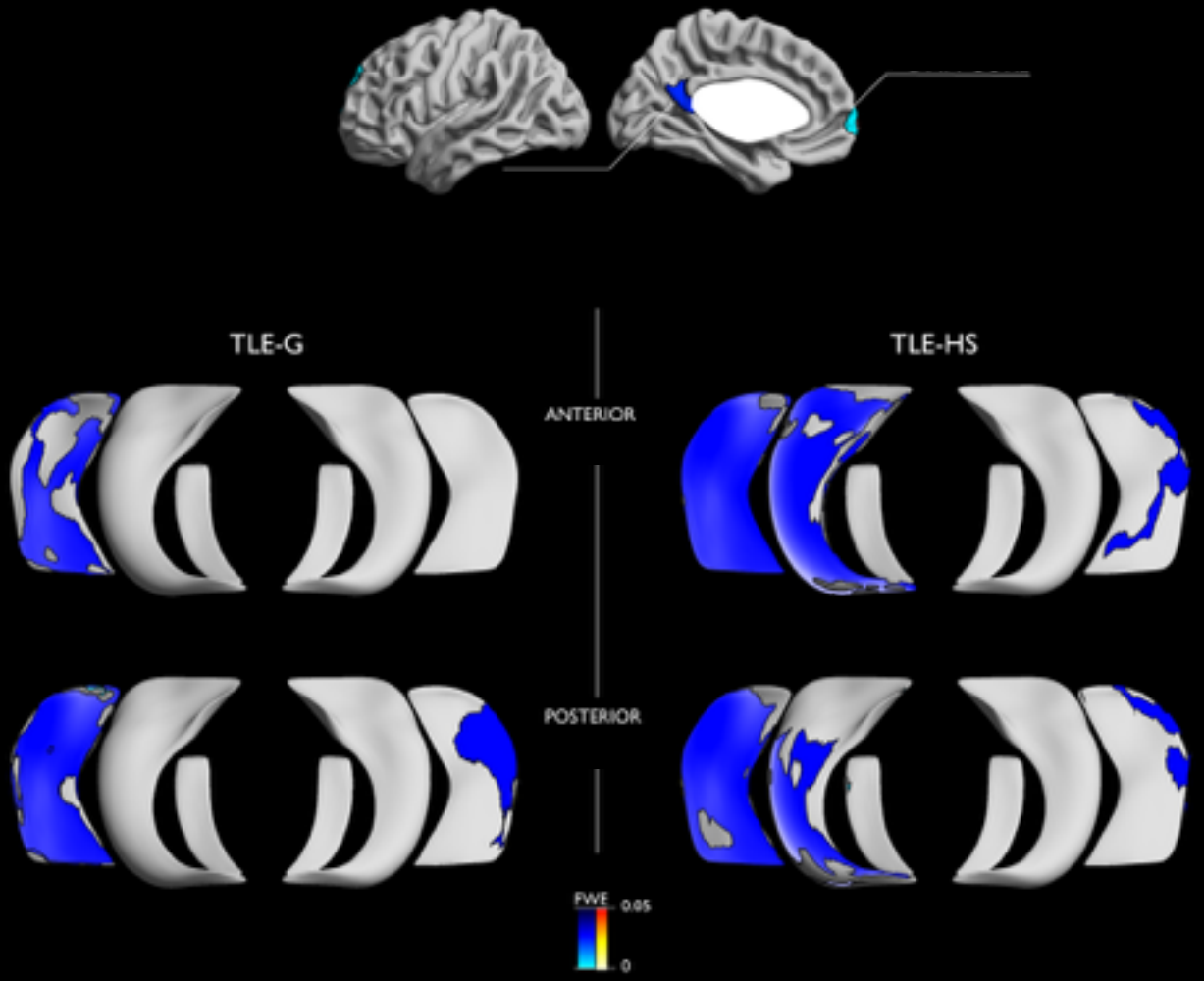


Andrews-Hanna et al (2010) Neuron

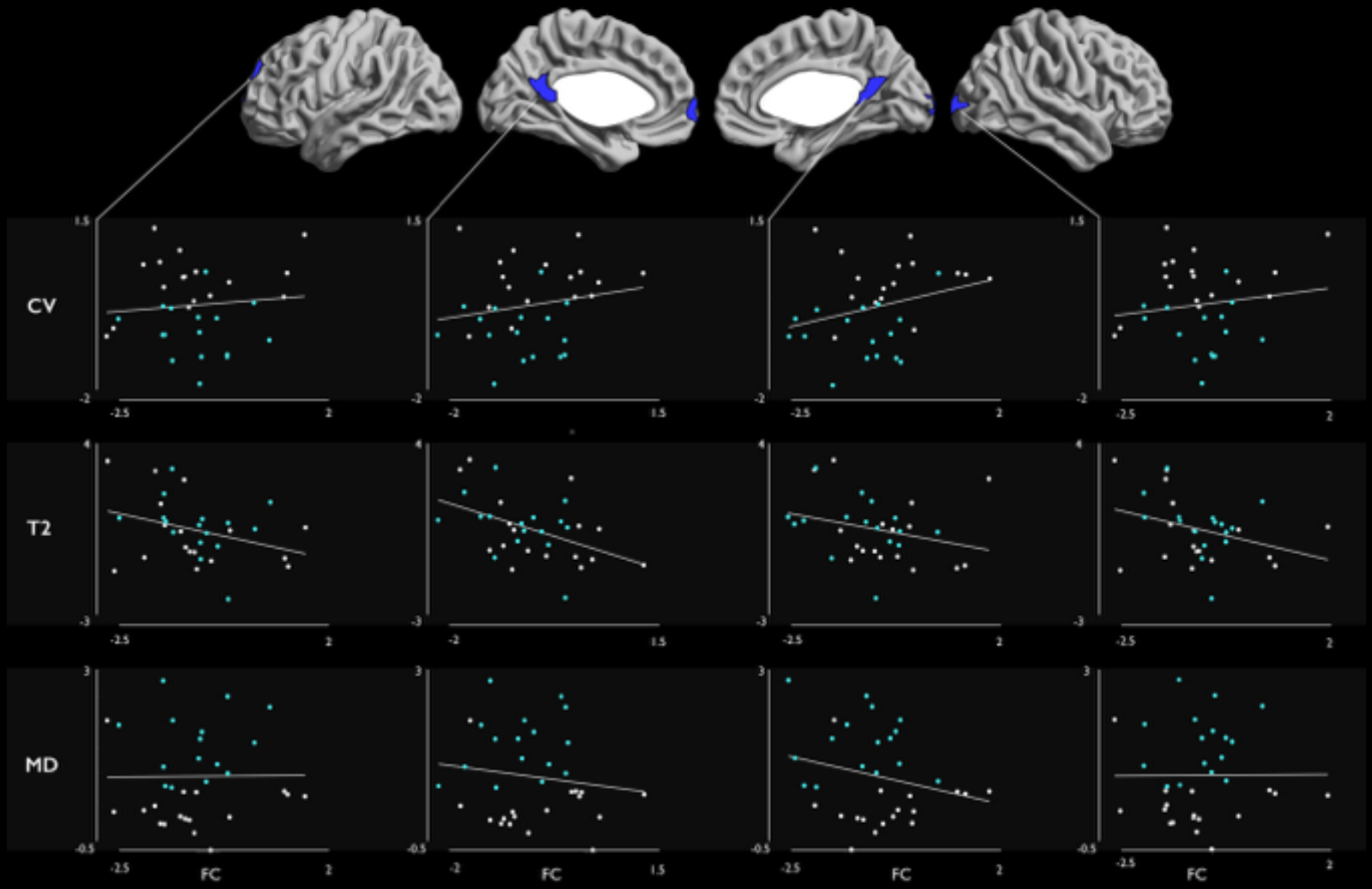
HIPPOCAMPAL–CORTICAL CONNECTIVITY ANOMALIES



INVERSE CONNECTIVITY MAPPING



STRUCTURE FUNCTION RELATIONSHIPS IN TLE



SUMMARY

Multimodal imaging of hippocampal subfield markers in TLE

Dissociation between pathologically defined patient subgroups at the level of

- Structural imaging profiles
- Functional embedding within DMN

Degree of structural anomalies relates to functional network markers

MOSTLY PROMISES…

MORE COMPREHENSIVE
IN VIVO HS DESCRIPTION

MORE PRECISE SURGICAL
TARGET DEFINITION

MAY COMPLEMENT EMERGING THERAPIES
(e.g. MINIMALLY INVASIVE SURGERY)

EPILEPSY AS MODEL DISEASE TO ASSESS
IMPACT OF LESIONS ON NETWORKS

PRE/POST-SURGICAL WORKUP:
OPPORTUNITIES FOR
BIOMARKER VALIDATION

Neuroimaging of Epilepsy Lab

Neda Bernasconi

Andrea Bernasconi

Jessie Kulaga Yoskovitz

Seok-Jun Hong

Min Liu

Benoit Caldairou

Neuro Epilepsy Group

Jeffrey Hall

Marie Christine Guiot

Robarts Research Institute

Maged Goubran

Ali Khan

Terry Peters