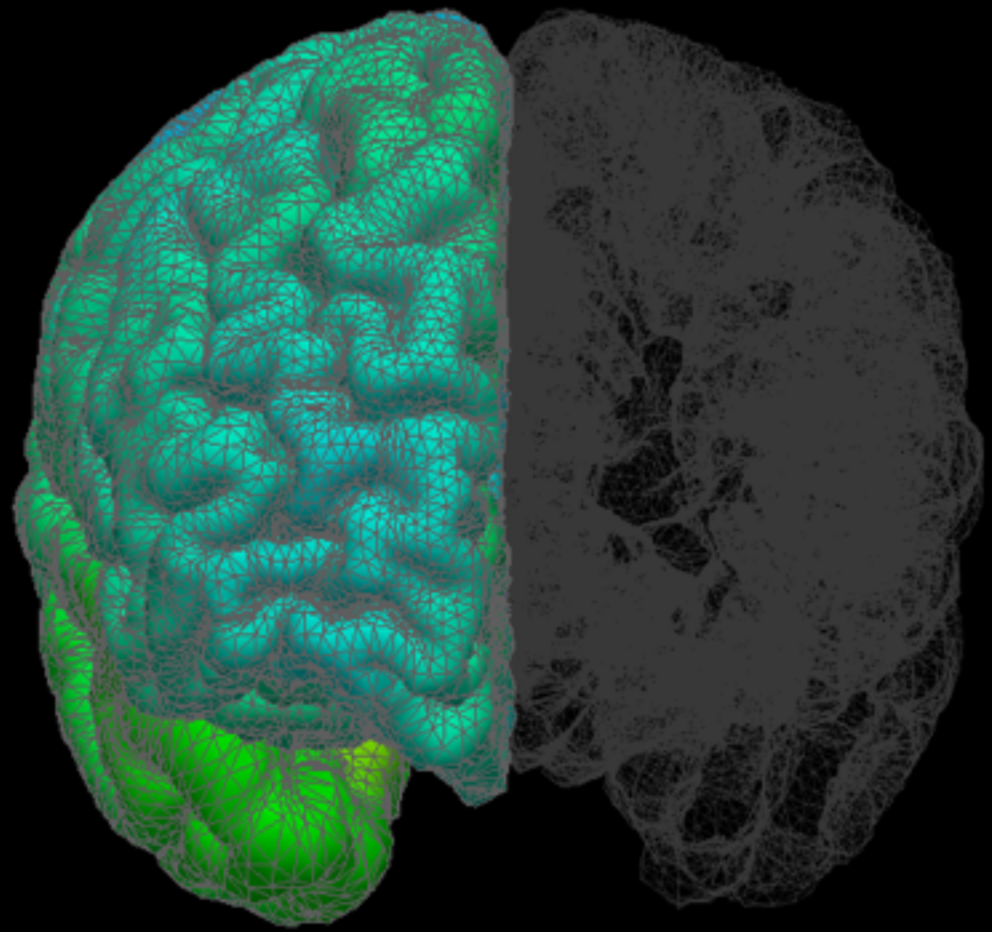


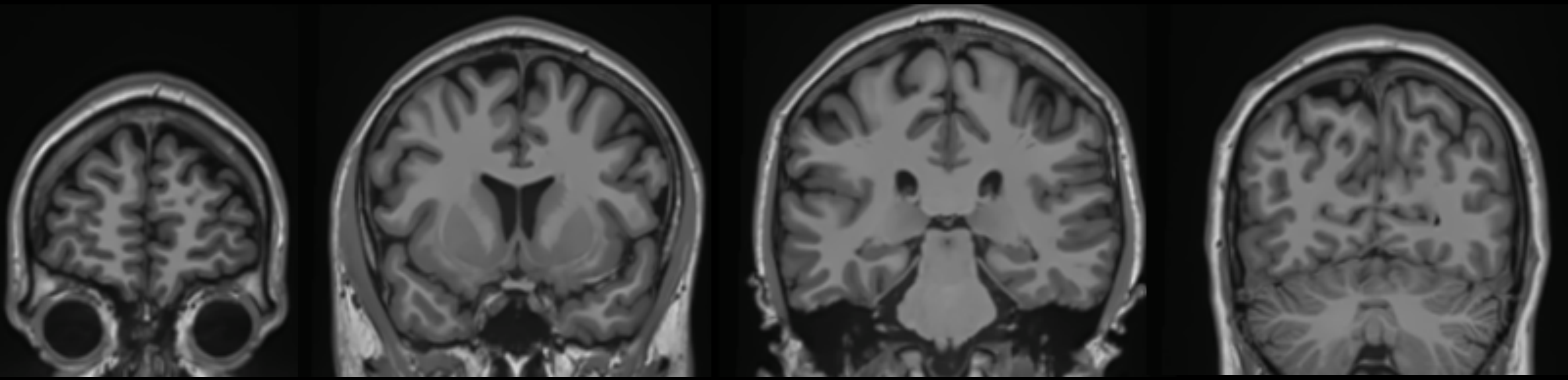
Structural MRI analysis

Boris Bernhardt, PhD

NeuroImaging of Epilepsy Lab

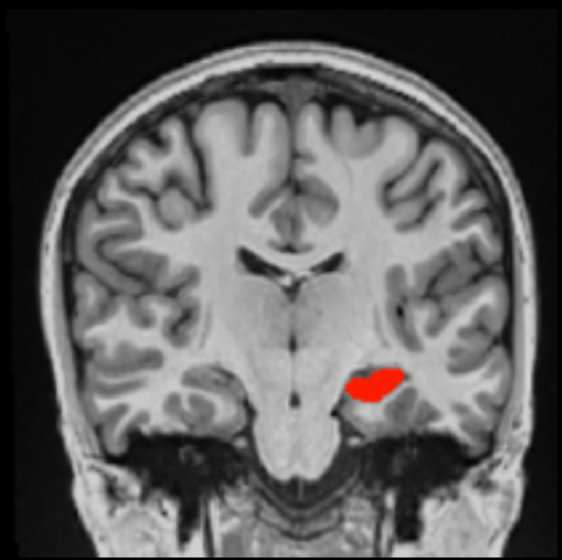
boris@bic.mni.mcgil.ca

structural MRI

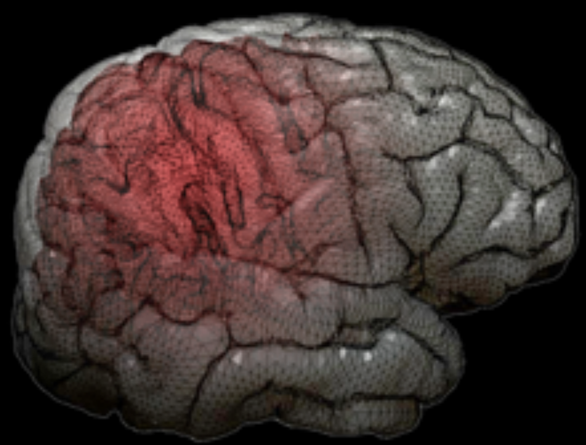


T1-weighted MRI

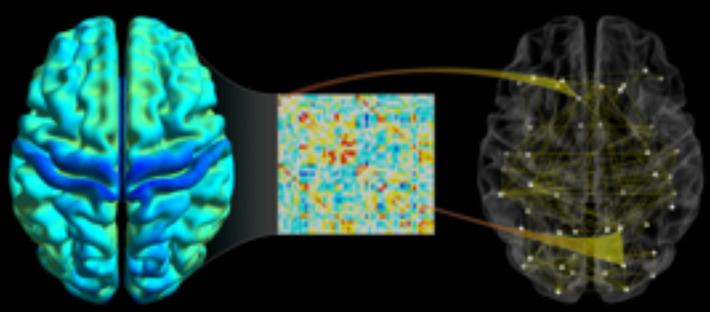
methods



MRI volumetry

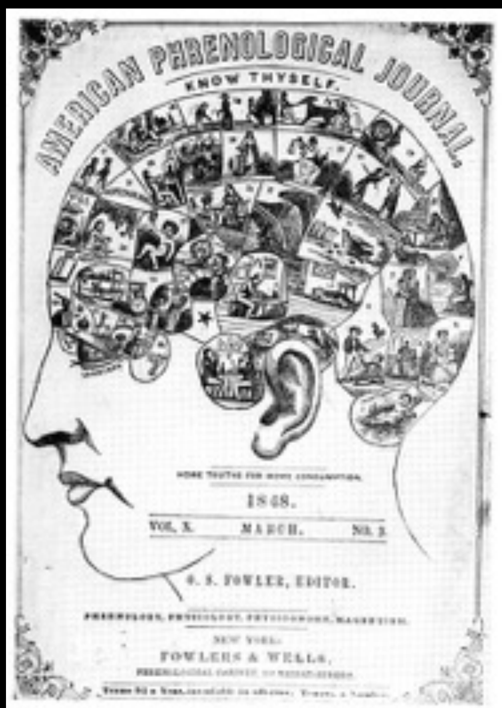


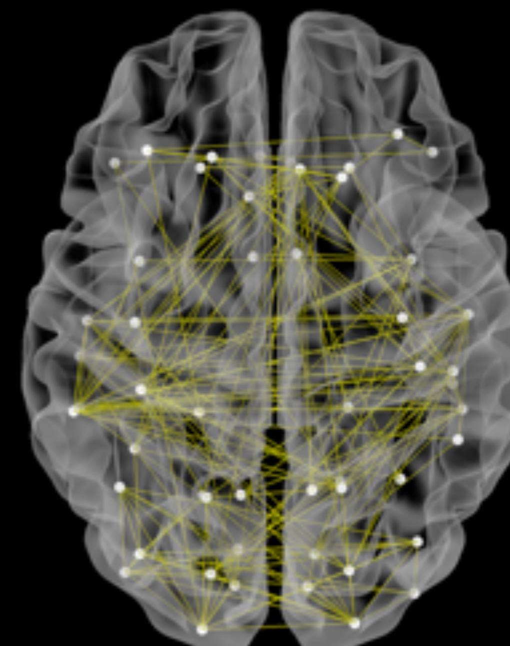
Surface-based analysis



Covariance mapping

applications

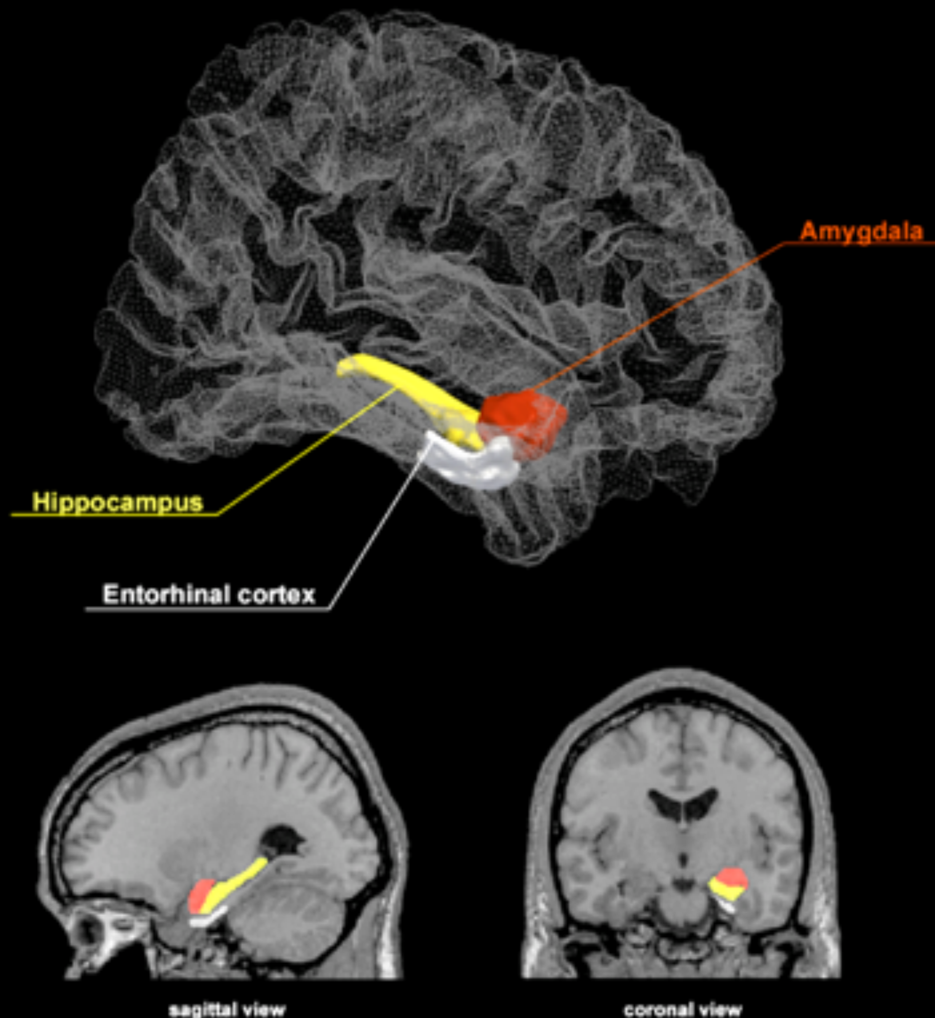




Individual differences

Brain disorders

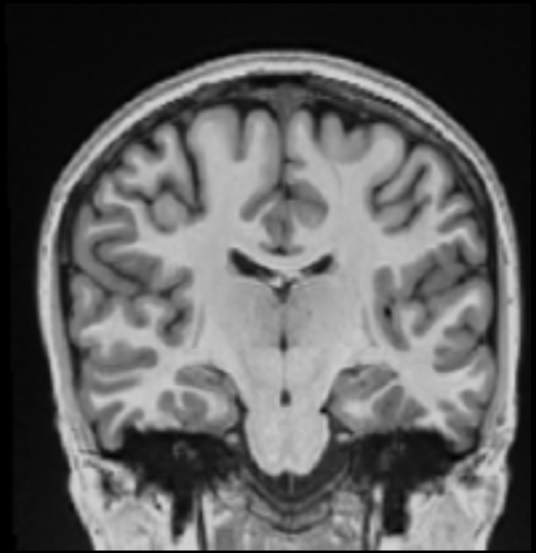
Brain organization

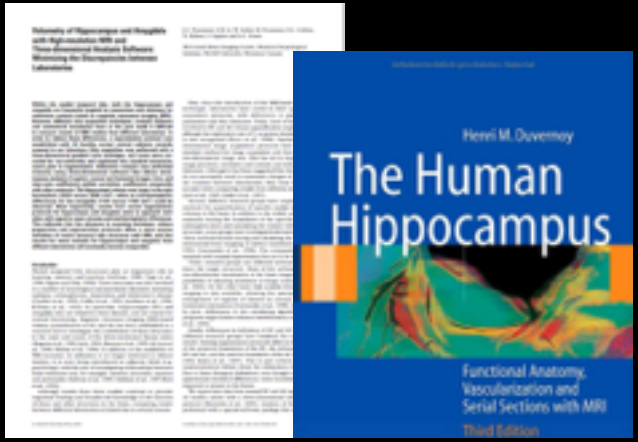


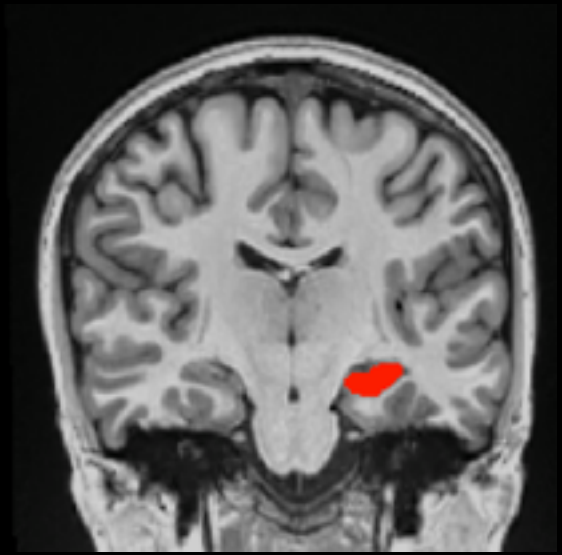
MRI volumetry

idea: trace structure in 3D and count number of voxels

volumetry 'pipeline'





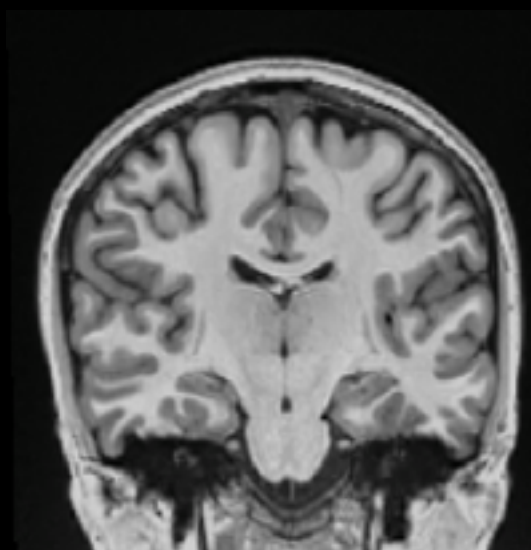


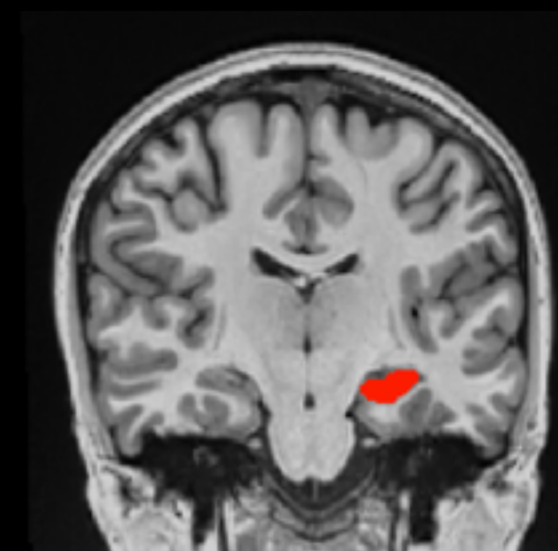
input

read and become expert

segment

alternative volumetry 'pipeline'





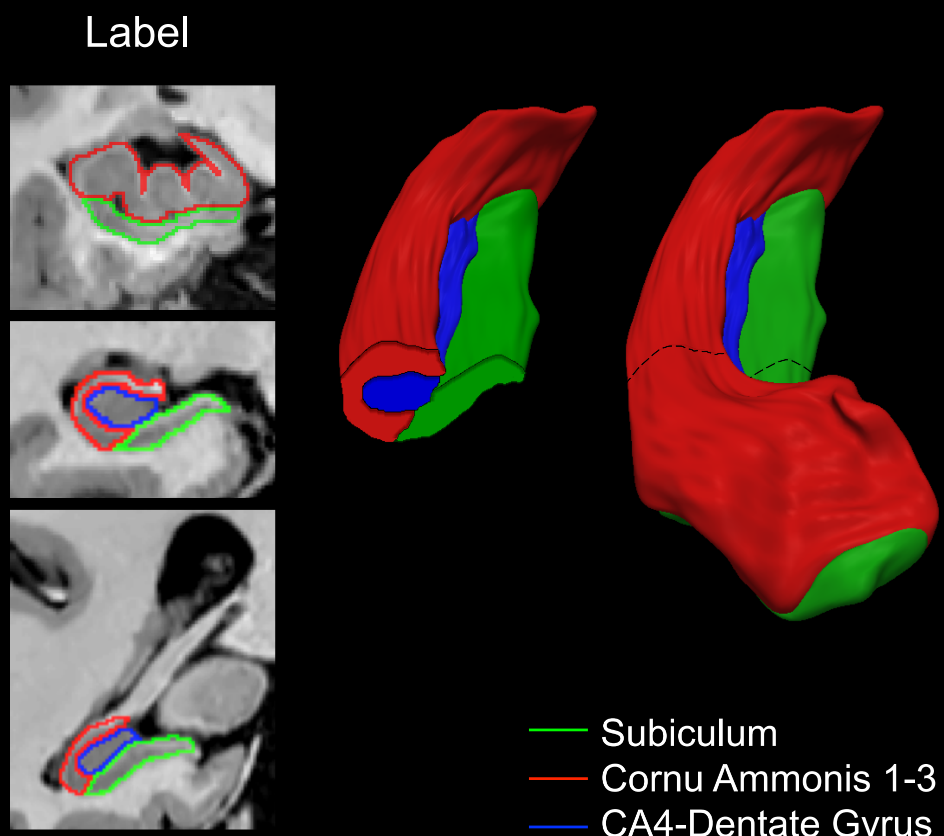
input automatic segmentation approaches segment

Chupin et al. (2009) NeuroImage

Coupe et al. (2010) MICCAI

Kim et al. (2011) MedImaAnal

subfield volumetry



Kulaga-Yoskovitz and Bernasconi

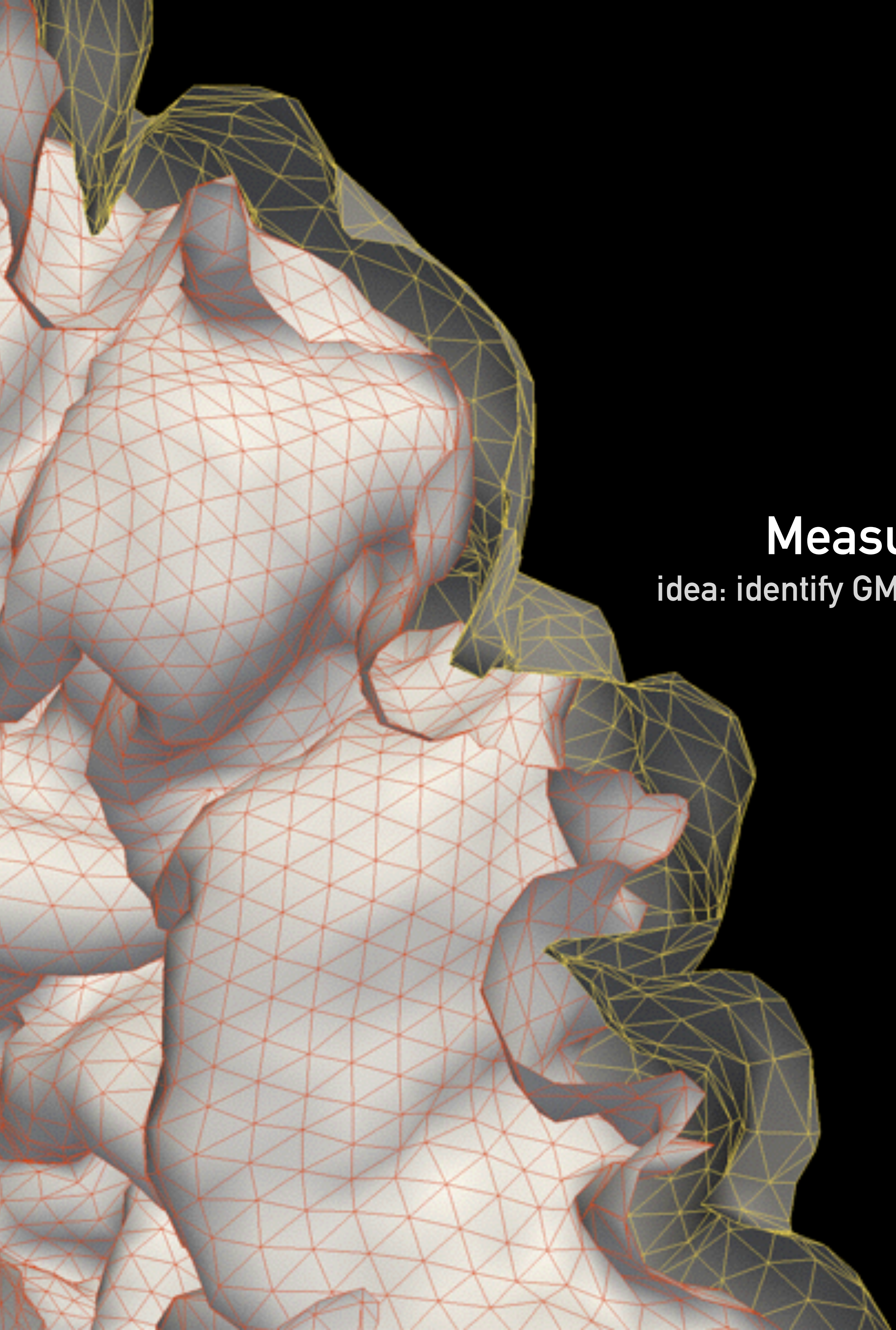
MRI volumetry: pros and cons

Pros

- focussed, simple methodology
- biologically and anatomically meaningful
- clinically well established
- subregional level of analysis possible

Cons

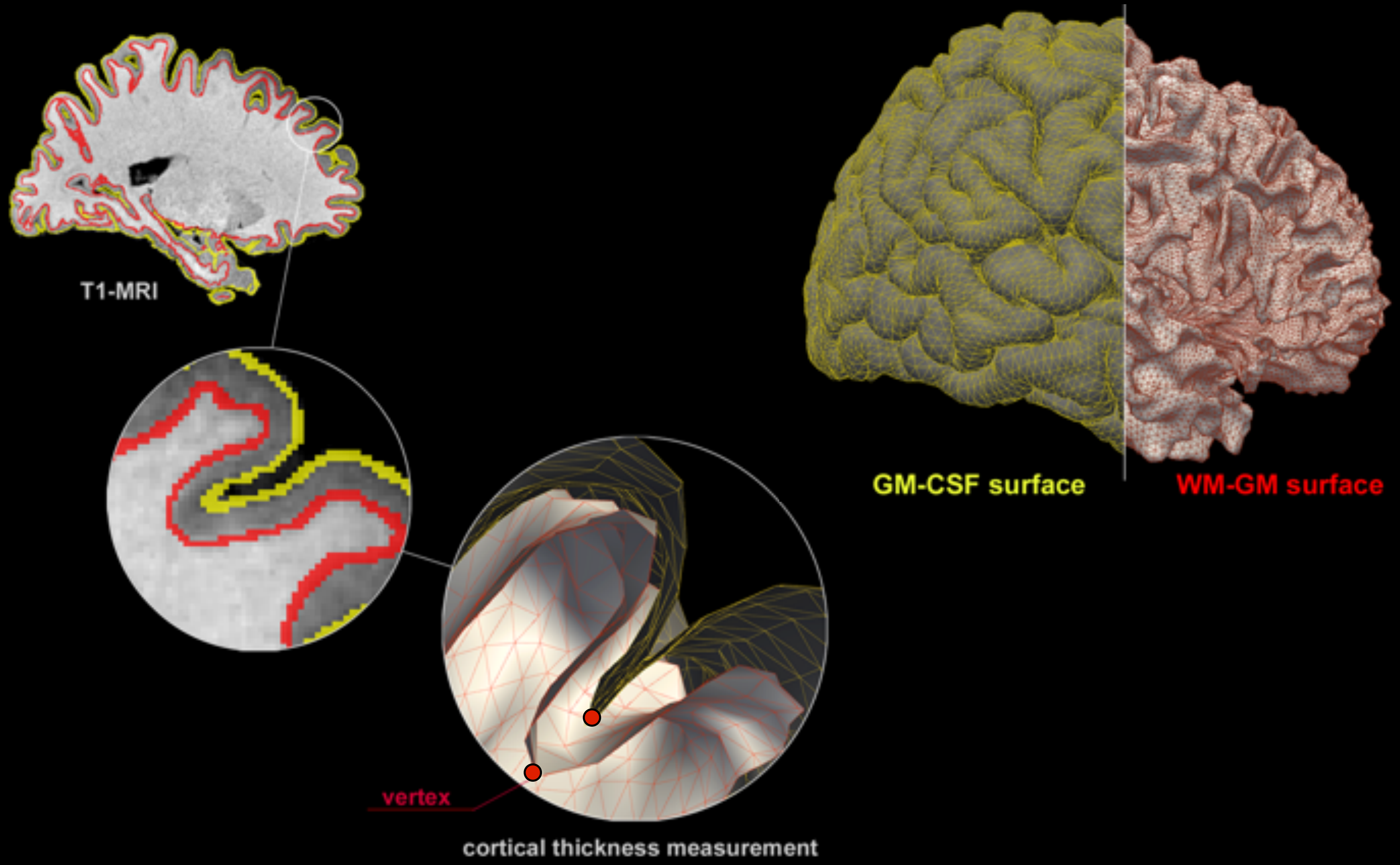
- labor-intensive manual segmentations are gold standard
- requires expert anatomical knowledge
- inter-rater, intra-rater variability, inter-protocol variability
- limited to individual anatomical regions



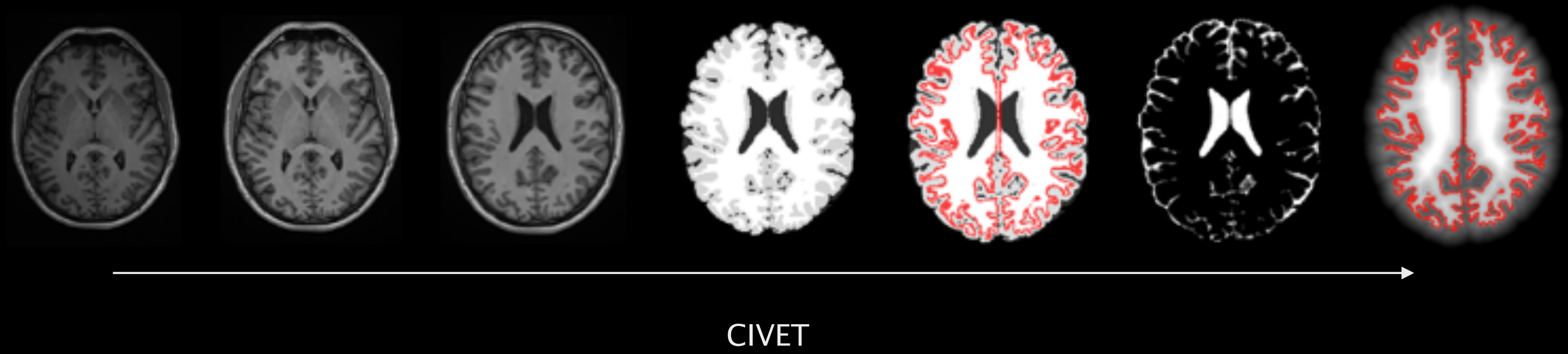
Measuring cortical thickness on MRI

idea: identify GM/WM and GM/CSF, measure their distance

MRI-based cortical thickness measurements



some processing...

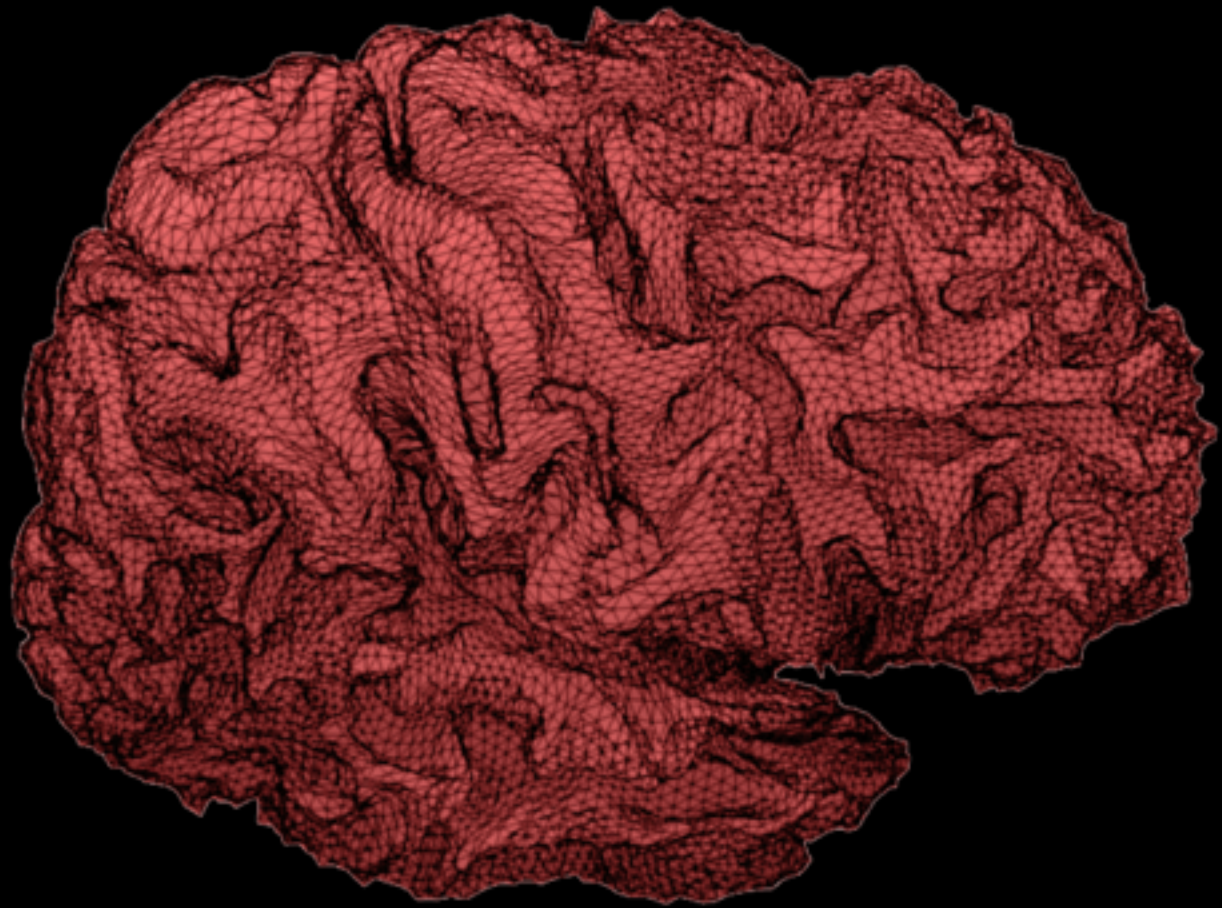


OMM: March 17

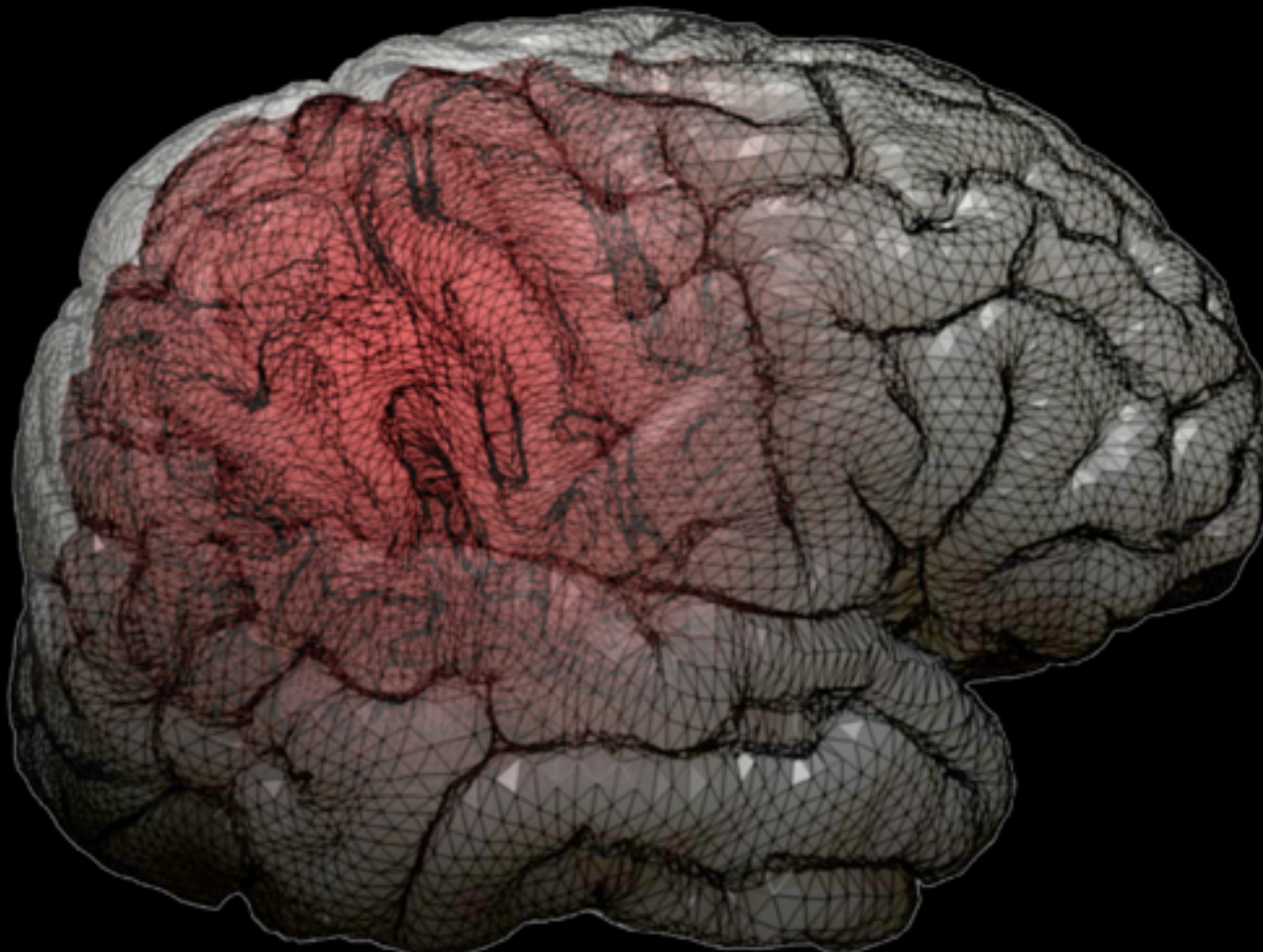
MacDonald et al. (2000) NeuroImage

Kim et al. (2005) NeuroImage

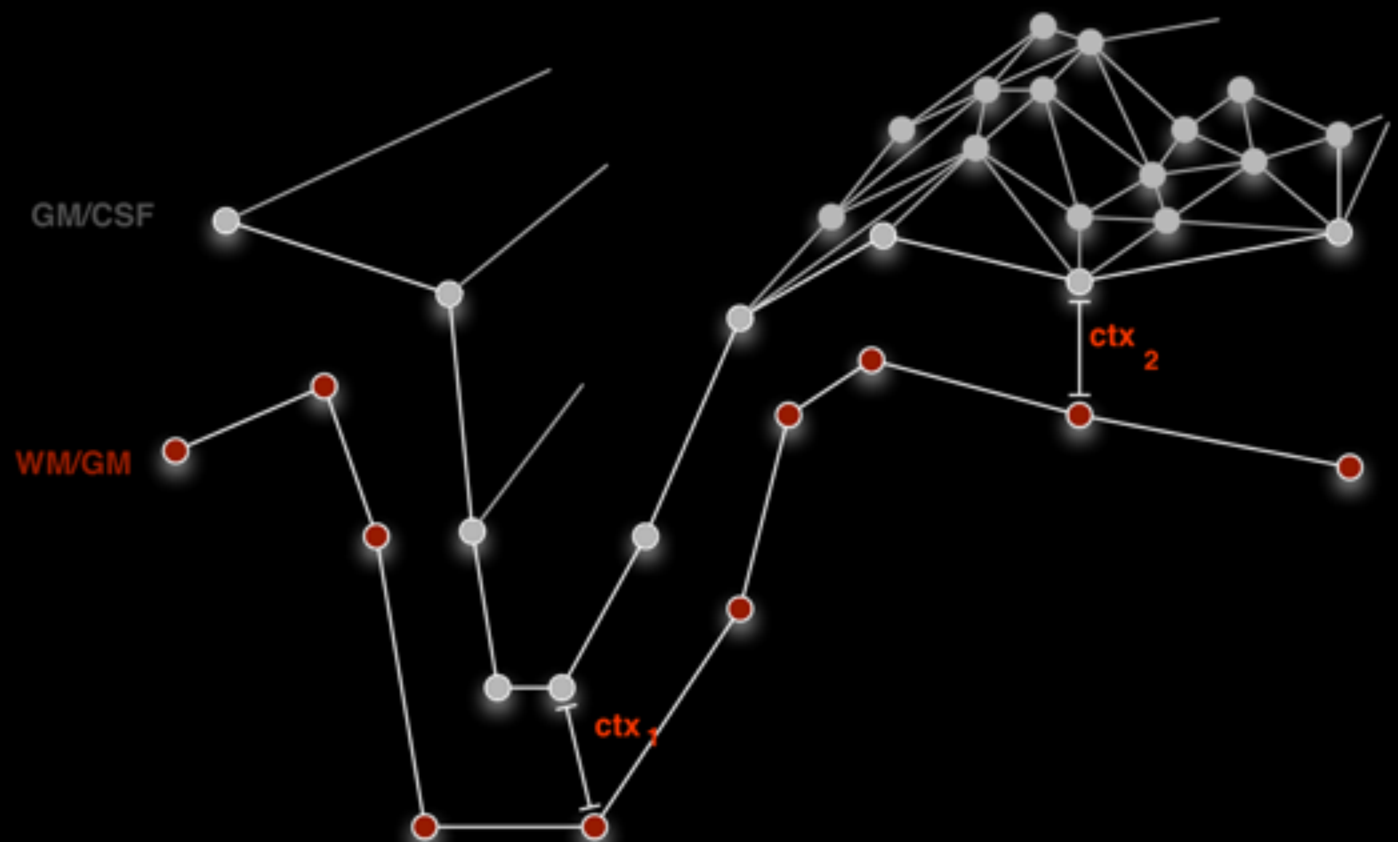
WM surface



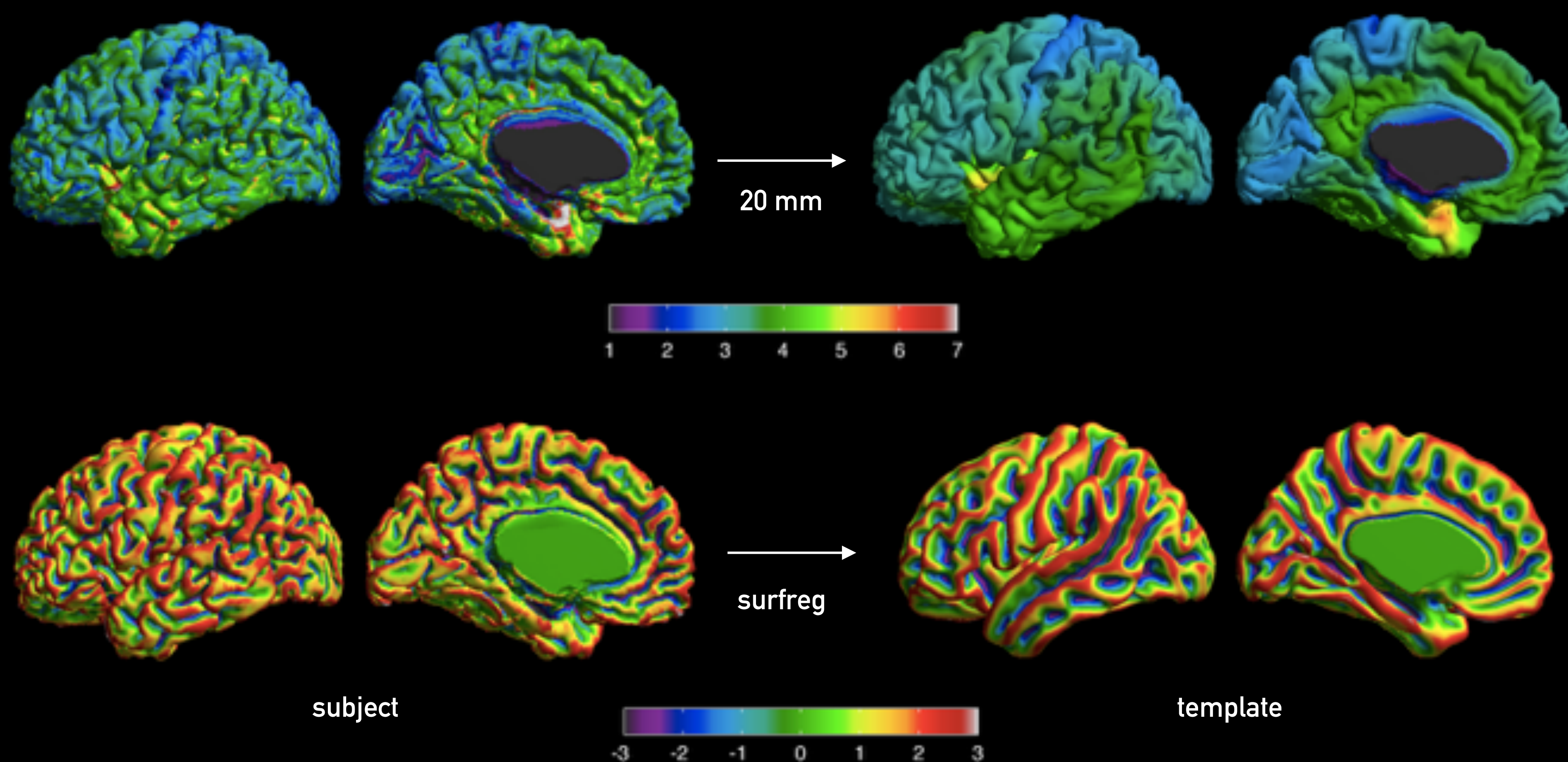
GM surface



measurement of cortical thickness

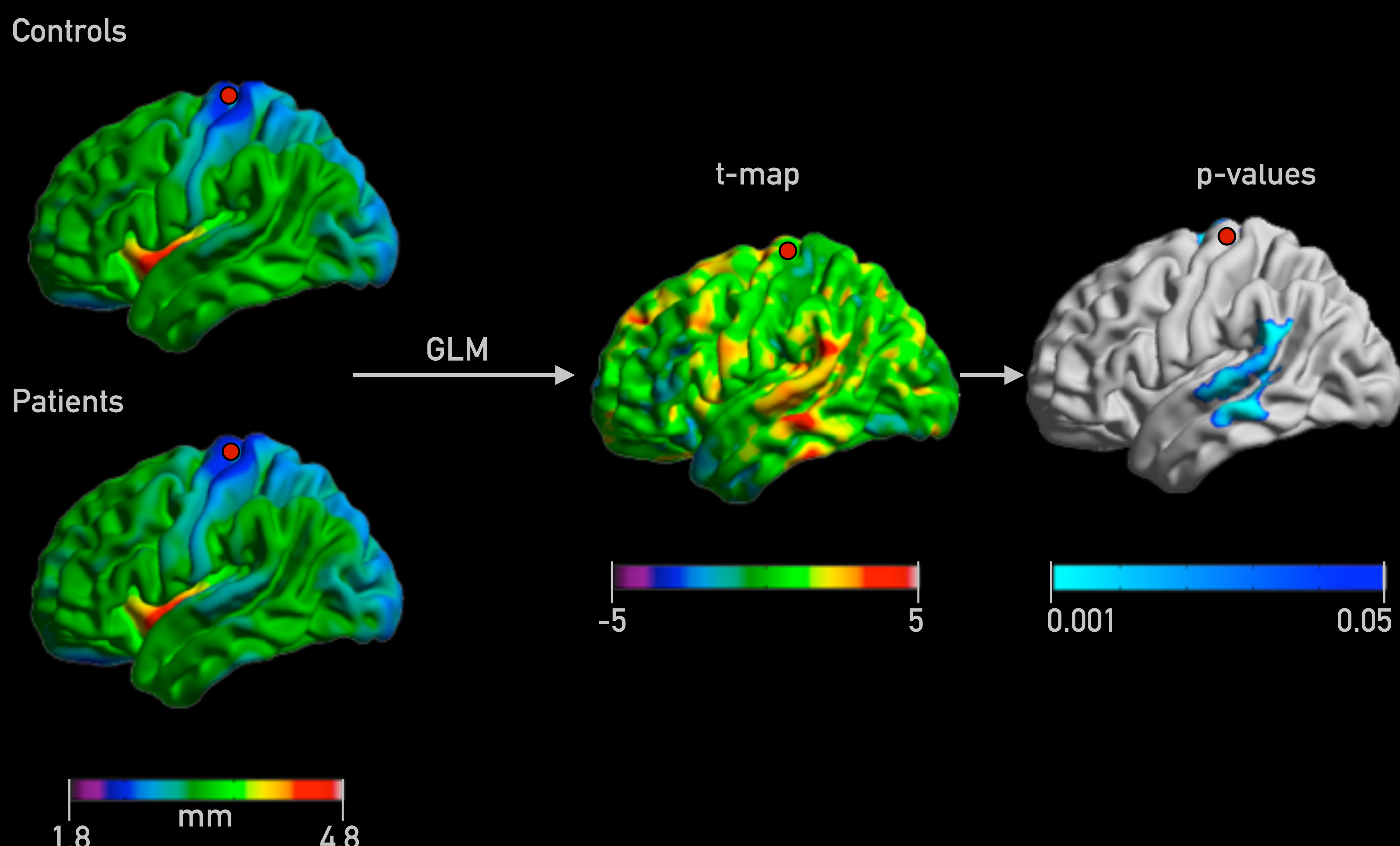


surface-based processing



Chung et al. (2003) NeuroImage
Robbins et al. (2004) MedImaAnalysis

statistical analysis using SurfStat



http://www.math.mcgill.ca/keith/surfstat/

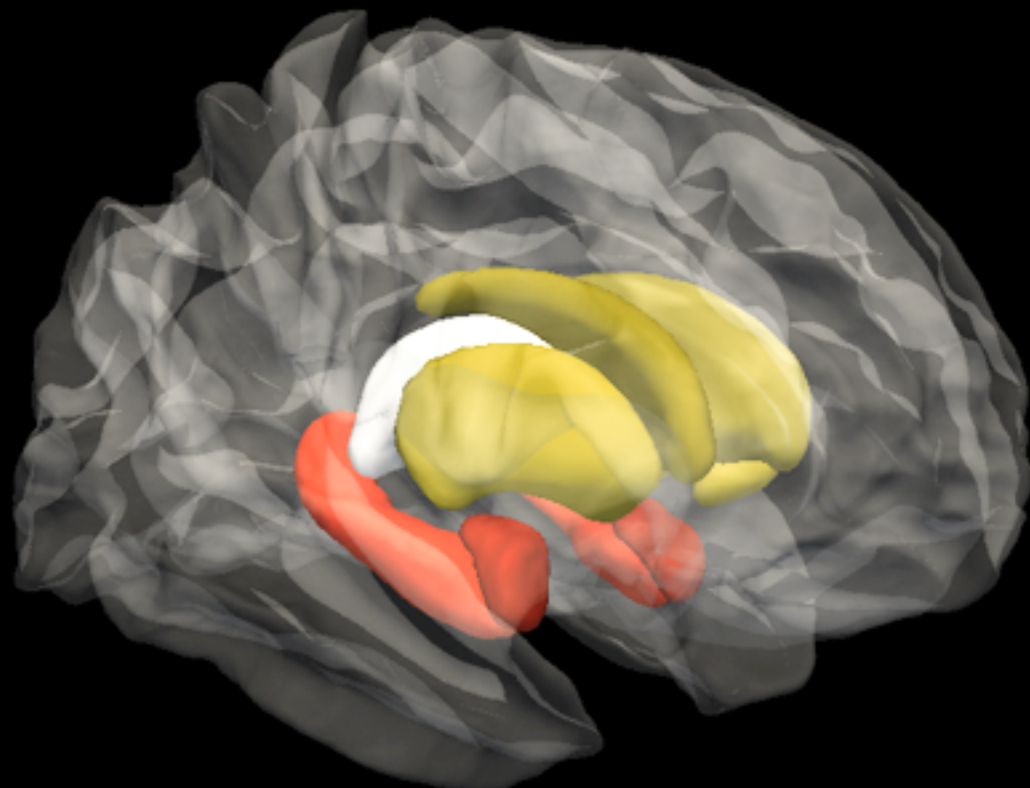
cortical thickness: pros and cons

Pros

- automated, continuous, whole-cortex
- processing and measurement respect cortical topology
- direct, biologically meaningful, mm-measure
- surface-registration may increase sensitivity

Cons

- heavy post-processing (4-25 hours/case)
- dependent on classification
- manual corrections often necessary
- limited to (neo)cortex

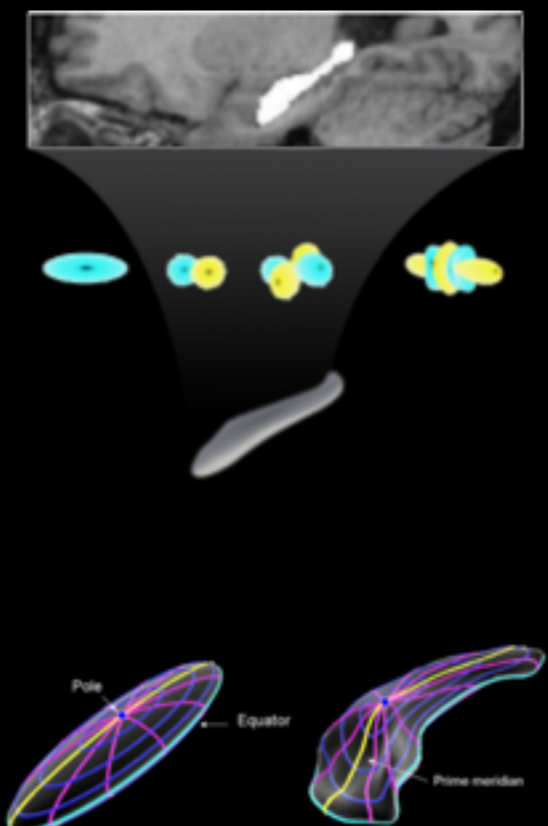


Surface-based analysis of subcortical shape

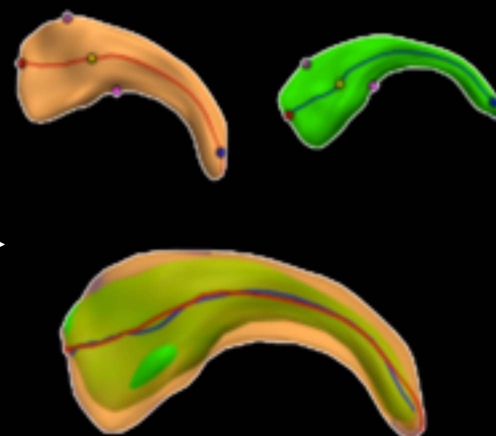
idea: take advantage of surface-based framework to assess subregional changes

SPHARM-PDM

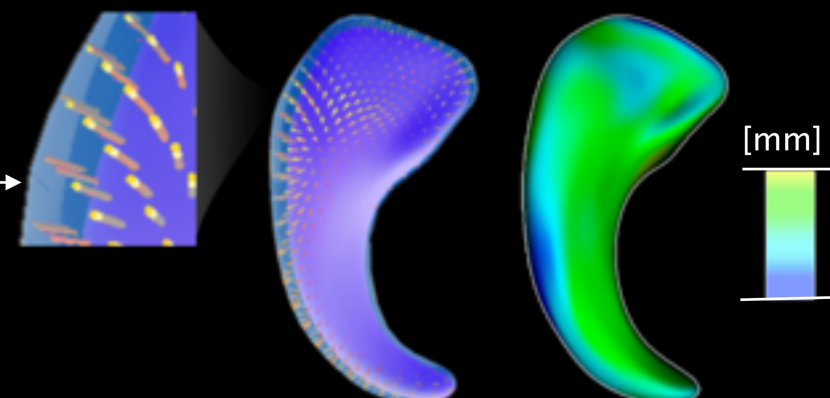
SPHARM-PDM



Alignment along long axis



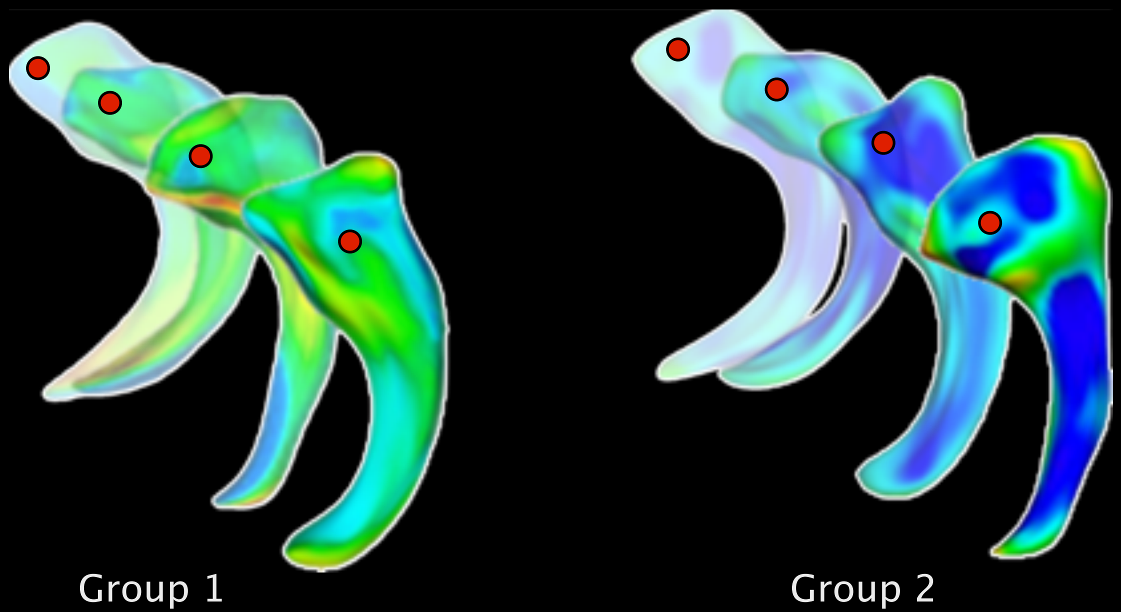
displacement from subject to template



Styner, Gerig et al. (2006), Kim et al. (2008)

http://pages.stat.wisc.edu/~mchung/research/amygdala/

statistical analysis with SurfStat



disp = 1 + GROUP + ε

disp = 1 + AGE + ε

http://www.math.mcgill.ca/keith/surfstat/

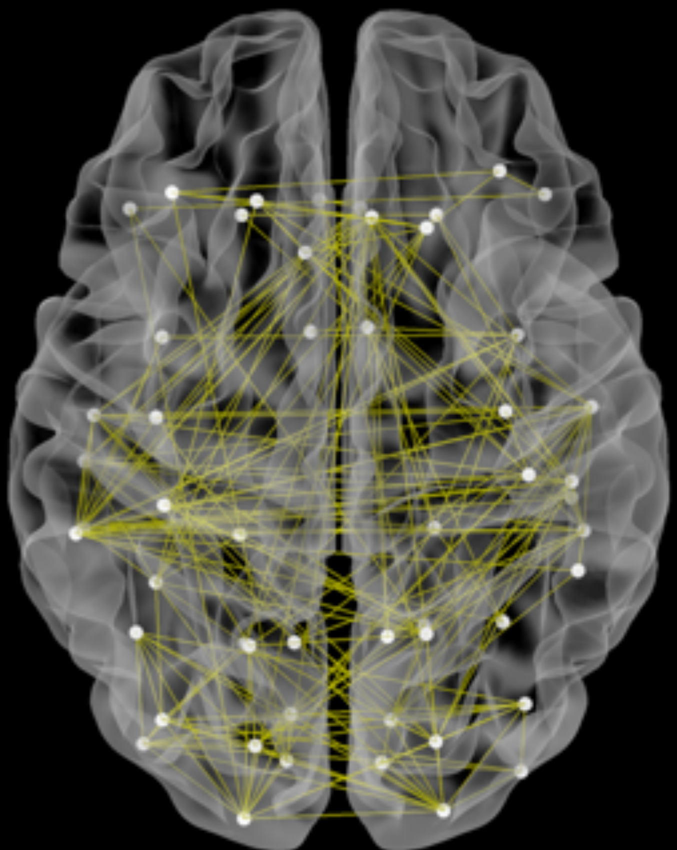
subcortical shape modeling: pros and cons

Pros

- subnuclear assessment possible
- intrinsic shape correspondence

Cons

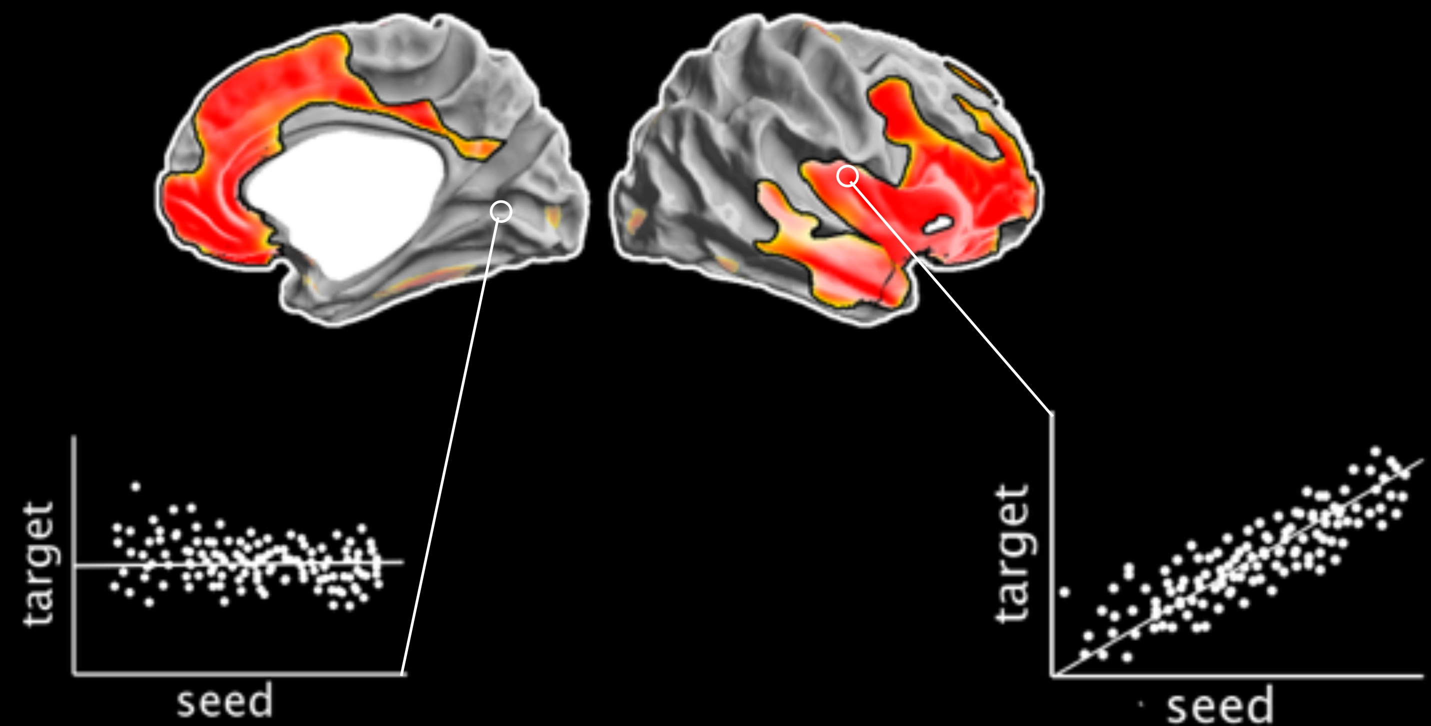
- good segmentations necessary (see volumetry)
- volumetric analysis limited to boundary regions



Structural covariance network mapping

idea: connections = structural correlations between regions across subjects

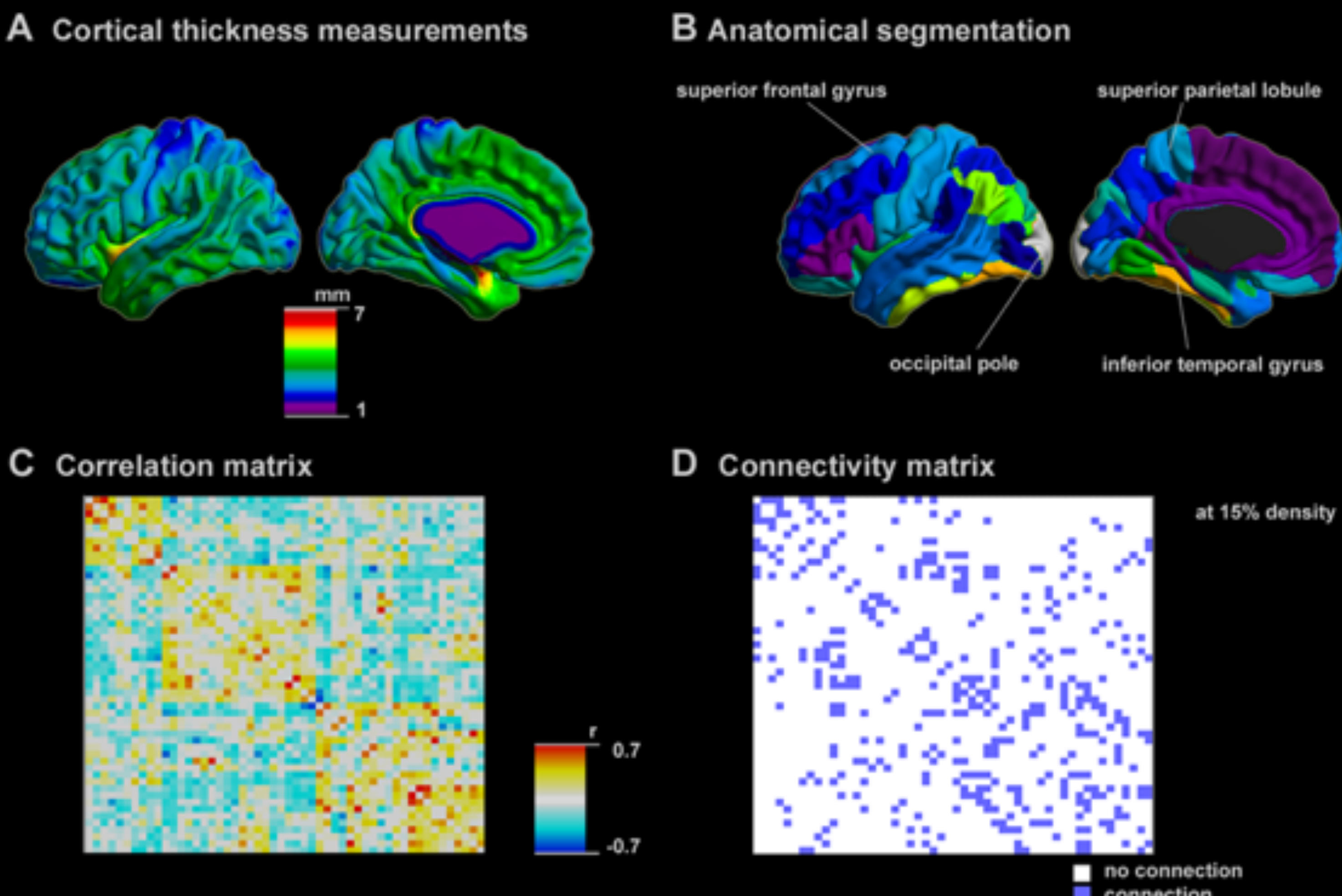
structural covariance network mapping

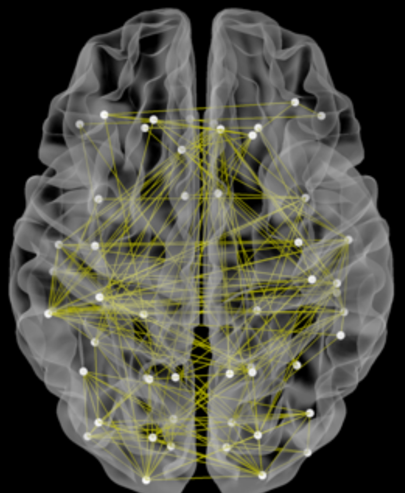


Lerch et al. (2006) NeuroImage

Alexander-Bloch et al. (2013) Nat Rev Neurosci

covariance network construction

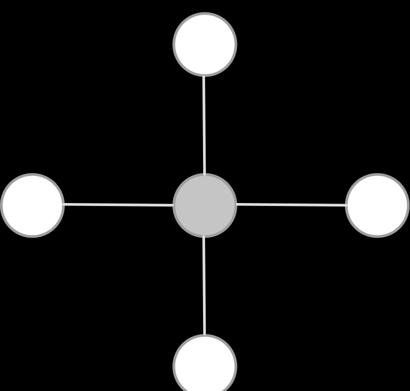




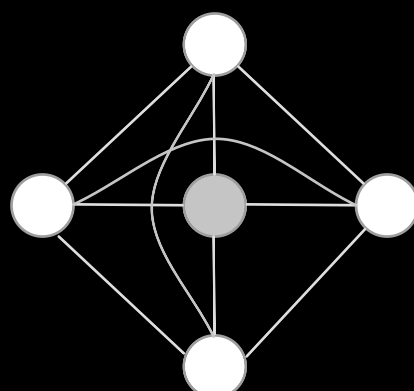
Bernhardt et al. (2011) CerCor

graph-theoretical network metrics

Clustering coefficient (C)

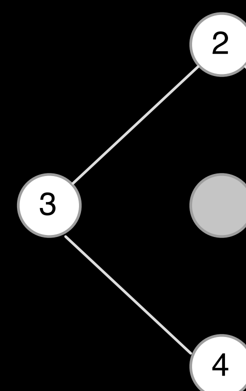


C = low

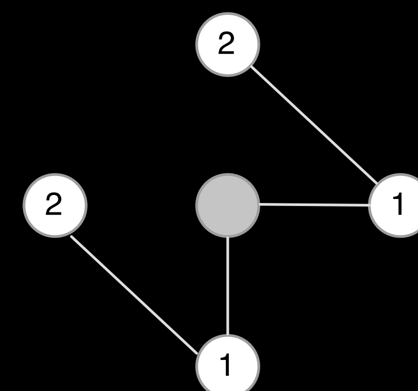


C = high

Characteristic path length (C)



L = high

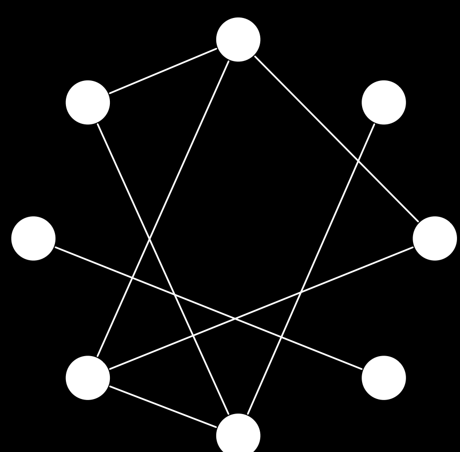


L = low

Watts and Strogatz (1998) Nature
Bullmore and Sporns (2009) Nat Rev Neurosci

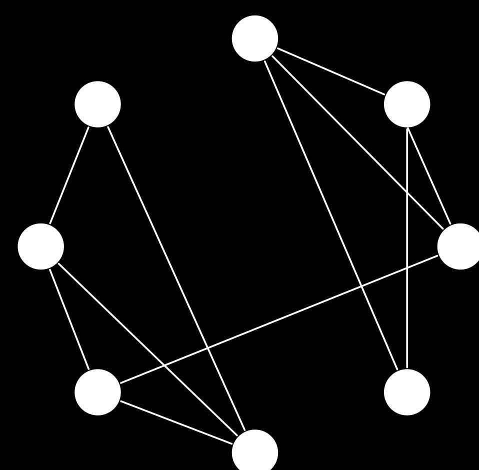
network topology

random network



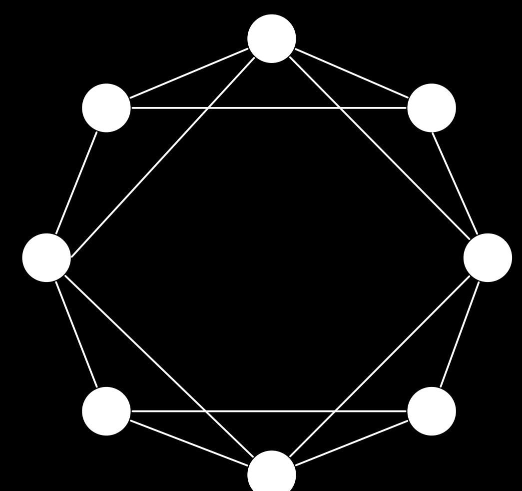
↓LP ↓CP

small-world regime



↓LP ↑CP

regular lattice network



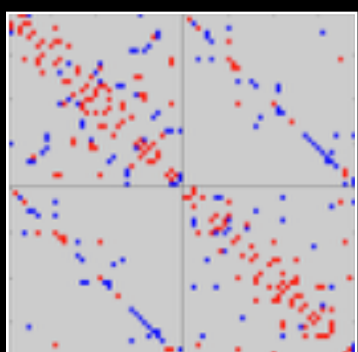
↑LP ↑CP

Watts and Strogatz (1998) Nature

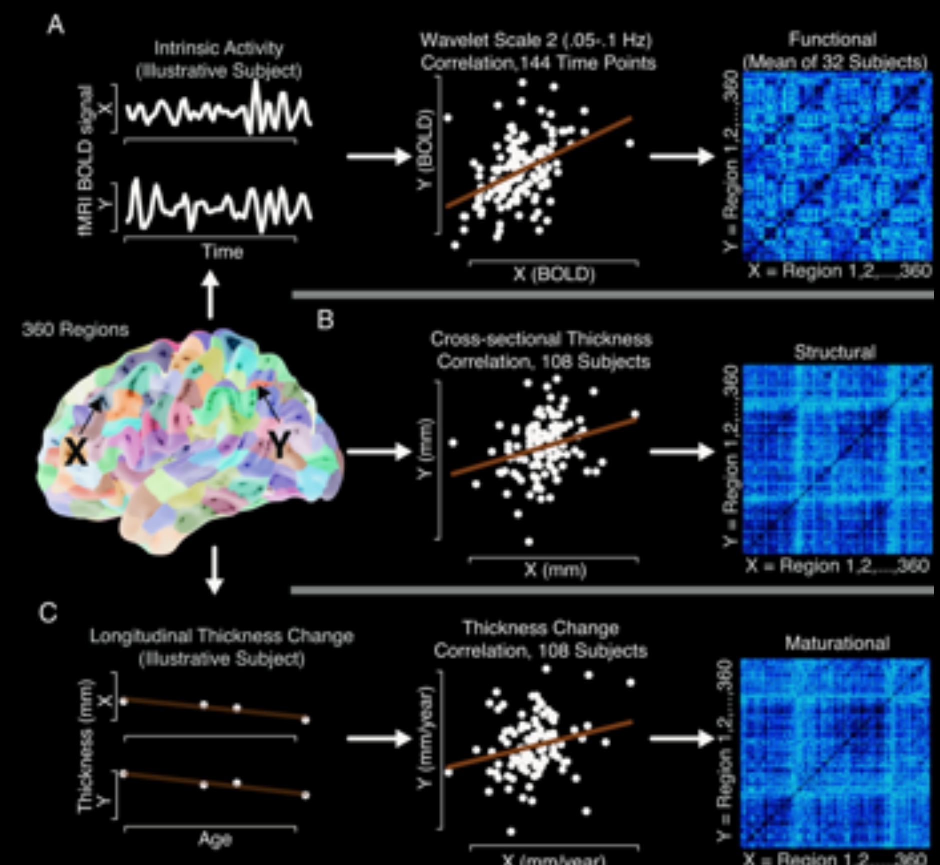
Bullmore and Sporns (2009) Nat Rev Neurosci

correspondence to other MRI networks

positive correlation



negative correlation



Gong, He, Chen, Evans (2010) NIMG

Alexander-Bloch, Bullmore, Giedd (2013) JNeurosci

structural covariance analysis: pros and cons

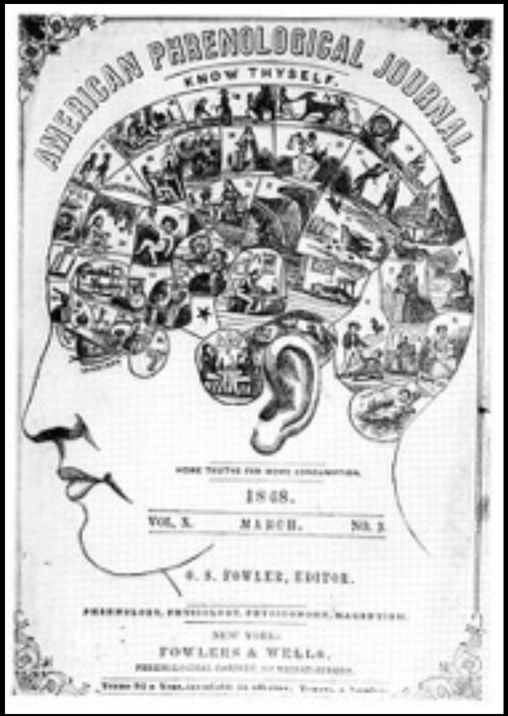
Pros

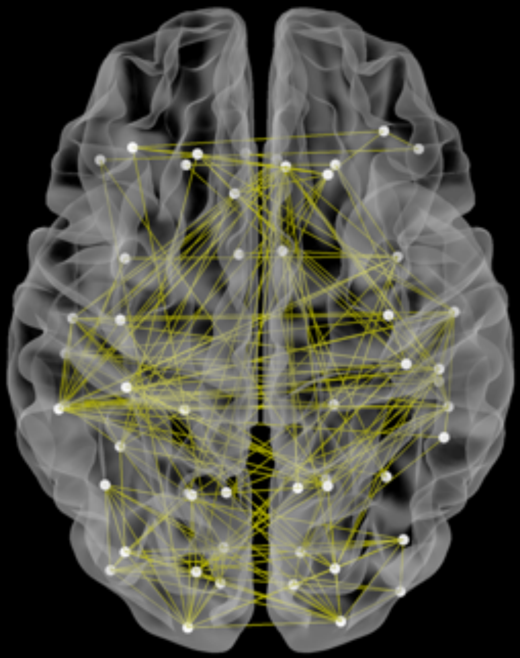
- relatively straightforward modeling
- seeding from within grey matter regions
- T1w-MRI less artifacts than epi-MRIs, higher resolution

Cons

- no direct correspondence with anatomical connections
  - *however*: process-based interpretation (e.g., maturation)
- restricted to group-level analysis (but see, Tijms et al. 2011)
- reviewers often request relatively large samples

applications





Individual differences

Brain disorders

Brain organization

Structural substrates of individual differences in cognitive functioning

MAX-PLANCK-GESELLSCHAFT

cognitive neuroscience

- assessed brain correlates of cognitive and affective processes
  - task-based
  - using functional MRI
  - localization of function
  - individual differences in cognitive skills

- *however*:
  - the biological basis of such differences incompletely understood
  - structural MRI has been underused to study cognition
  - off-task thought (aka mind-wandering) less frequently studied

mind-wandering

we constantly receive perceptual information; yet, we mind-wander

- can derail performance in challenging situations
- however: can be beneficial when demands of external world are low

previous work has shown links between mind-wandering and

... creativity, future thinking, and economic decision making (Smallwood et al.)

off-task thought relates to mPFC activity (Christoff 2009 PNAS)

mPFC activity also shown to relate to planning and temporal discounting
(Kable and Glimcher 2007 Nature; Schacter 2010 Neuron; Buckner 2009 TICS)

methods

to assess possibly adaptive mind-wandering

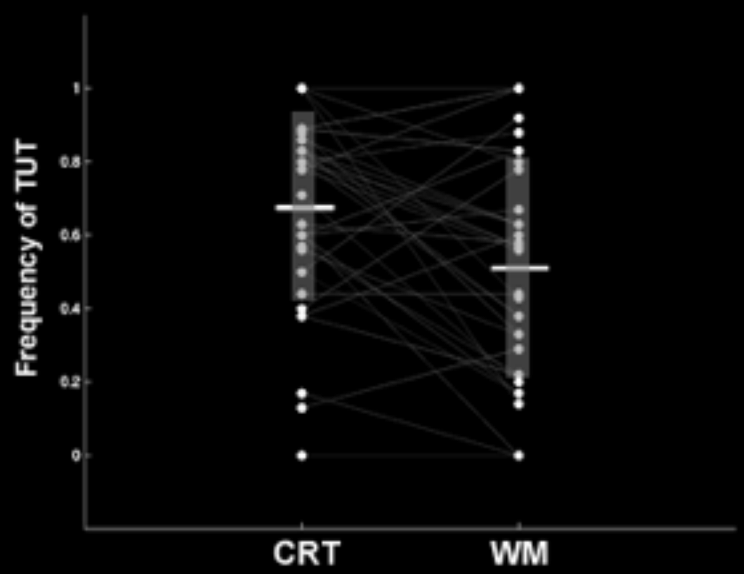
- task-unrelated thought during easy task (CRT) compared to hard task (WM)
- measure discounting as marker of patient decision-making

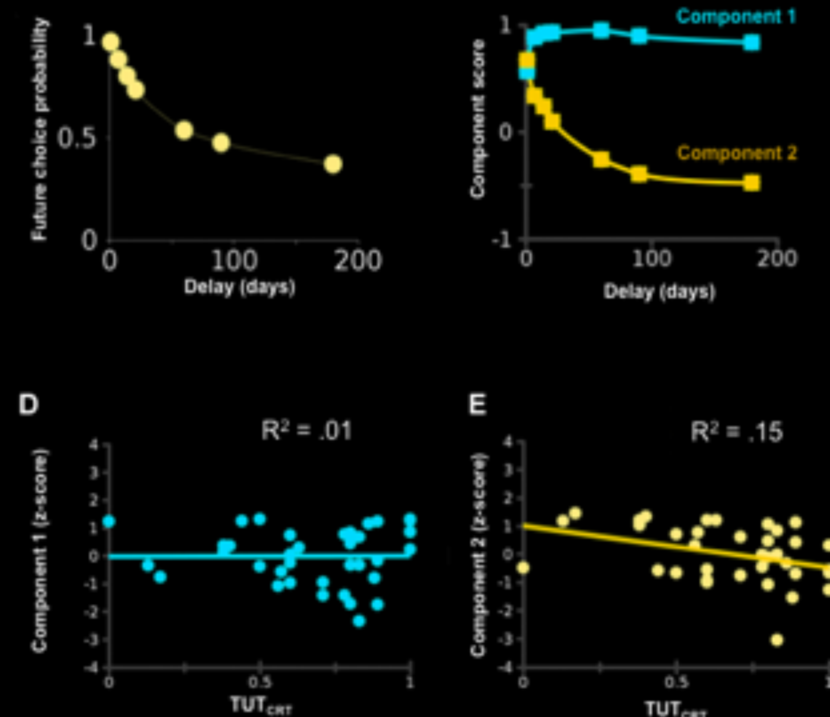
structural substrates of individual differences in tut and discounting

37 healthy controls; behavioral analysis; correlation with cortical thickness

mind-wandering and temporal discounting

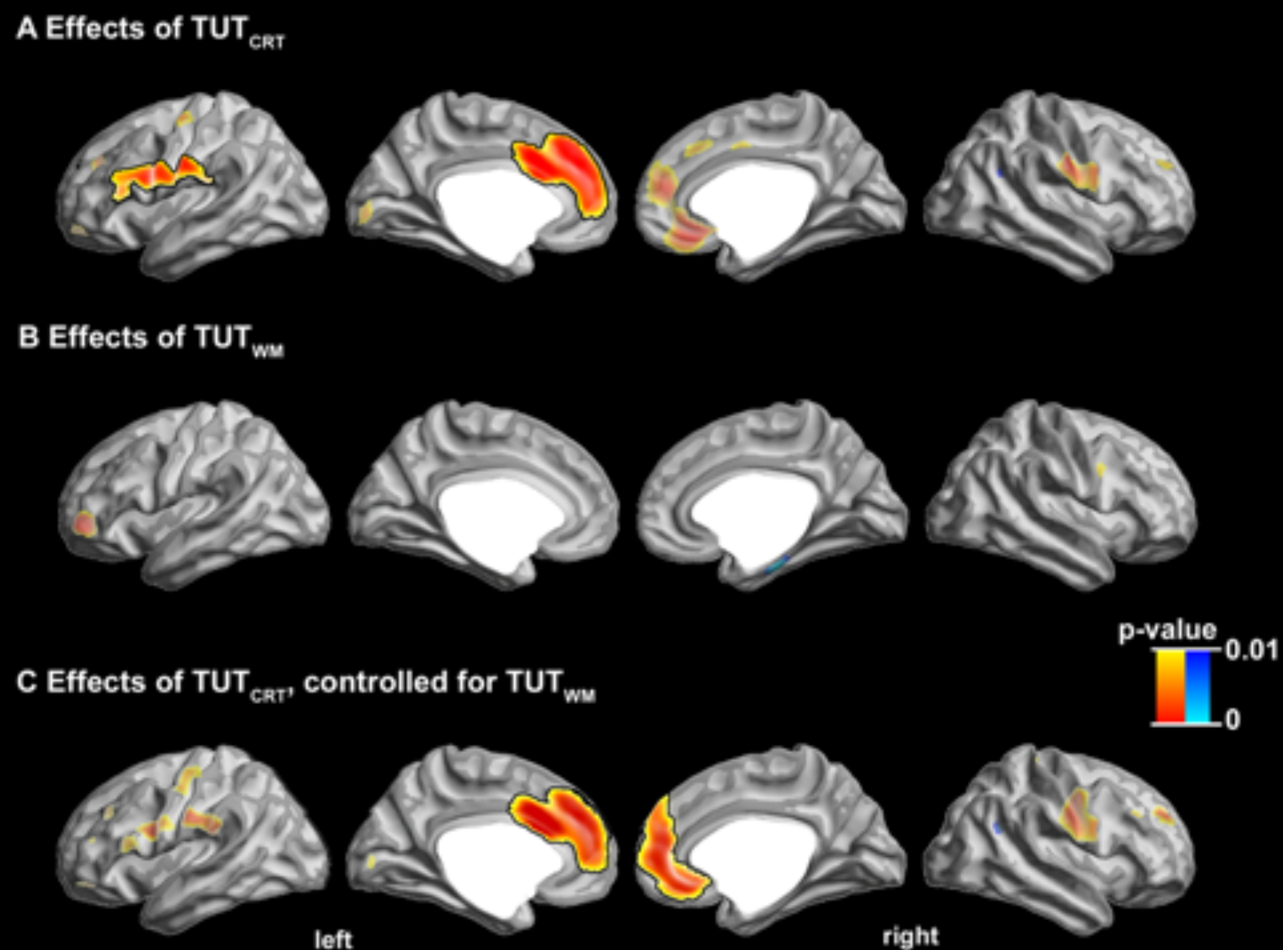
n=37





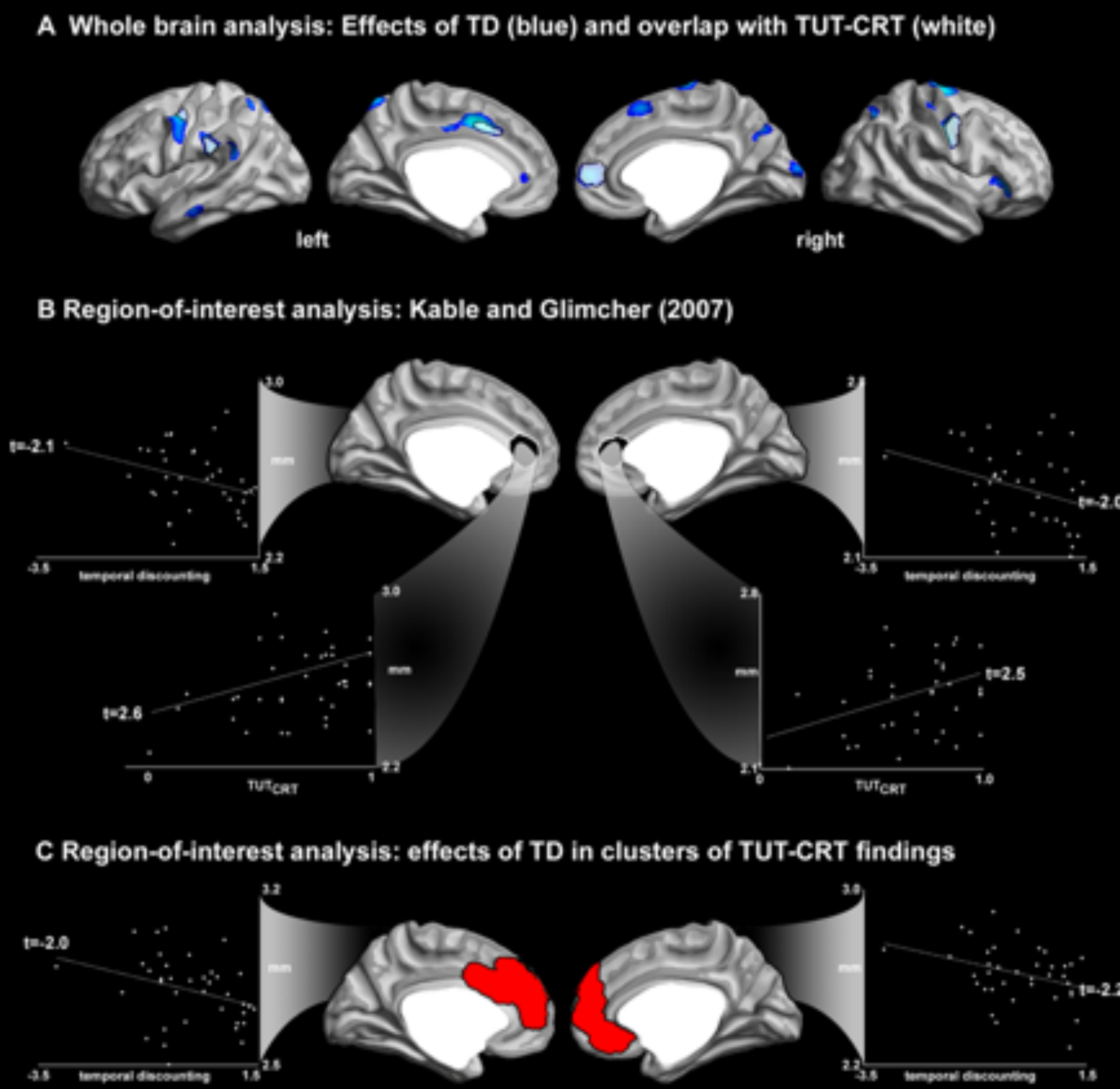
Bernhardt, Smallwood, et al. (2014) NIMG

substates of TUT



Bernhardt, Smallwood, et al. (2014) NIMG

overlap with substrates of discounting



conclusion

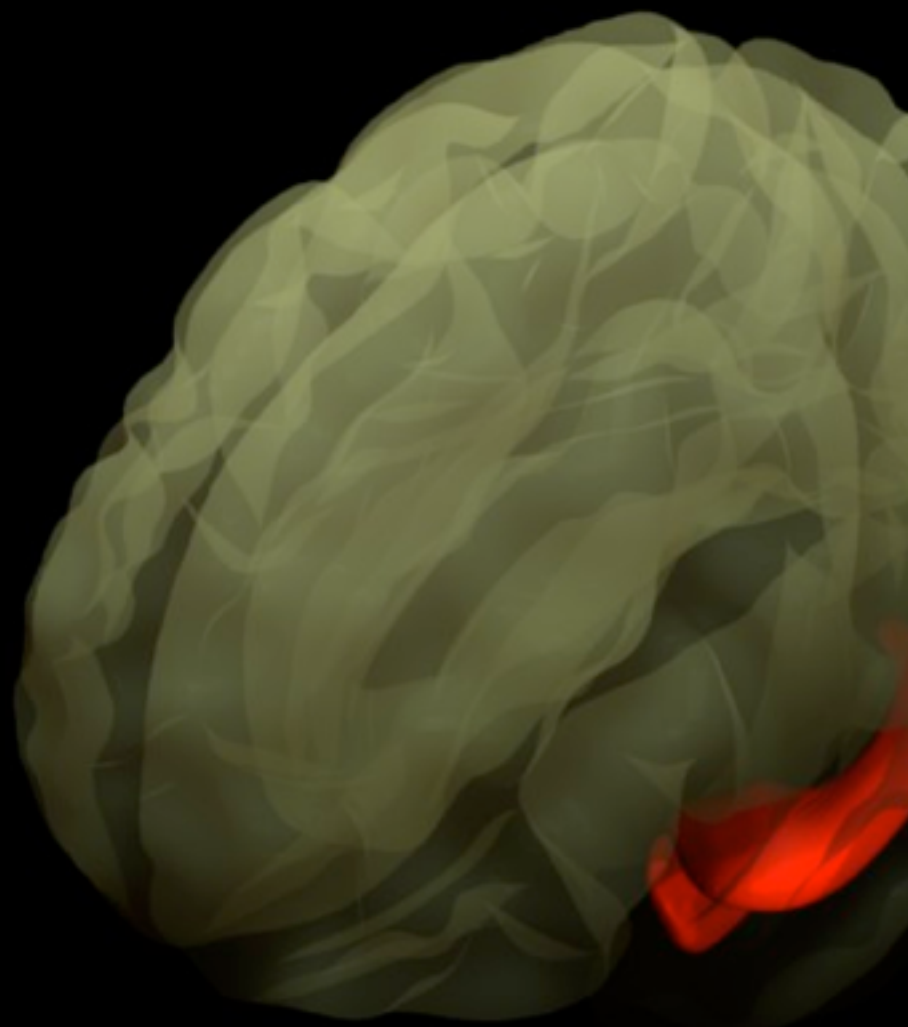
substrates of ability to adaptively decouple from here and now

- mind-wandering during easy but not hard task
- patient economic decision making

overlap in mPFC/ACC

- confirm functional MRI showing role of these regions in decoupled thought
- role in control / evaluation of information from memory
- self-projection (Buckner and Caroll 2009 TICS)
- mPFC/ACC strongly interconnected with mesiotemporal memory systems

Structural MRI analyses
in temporal lobe epilepsy

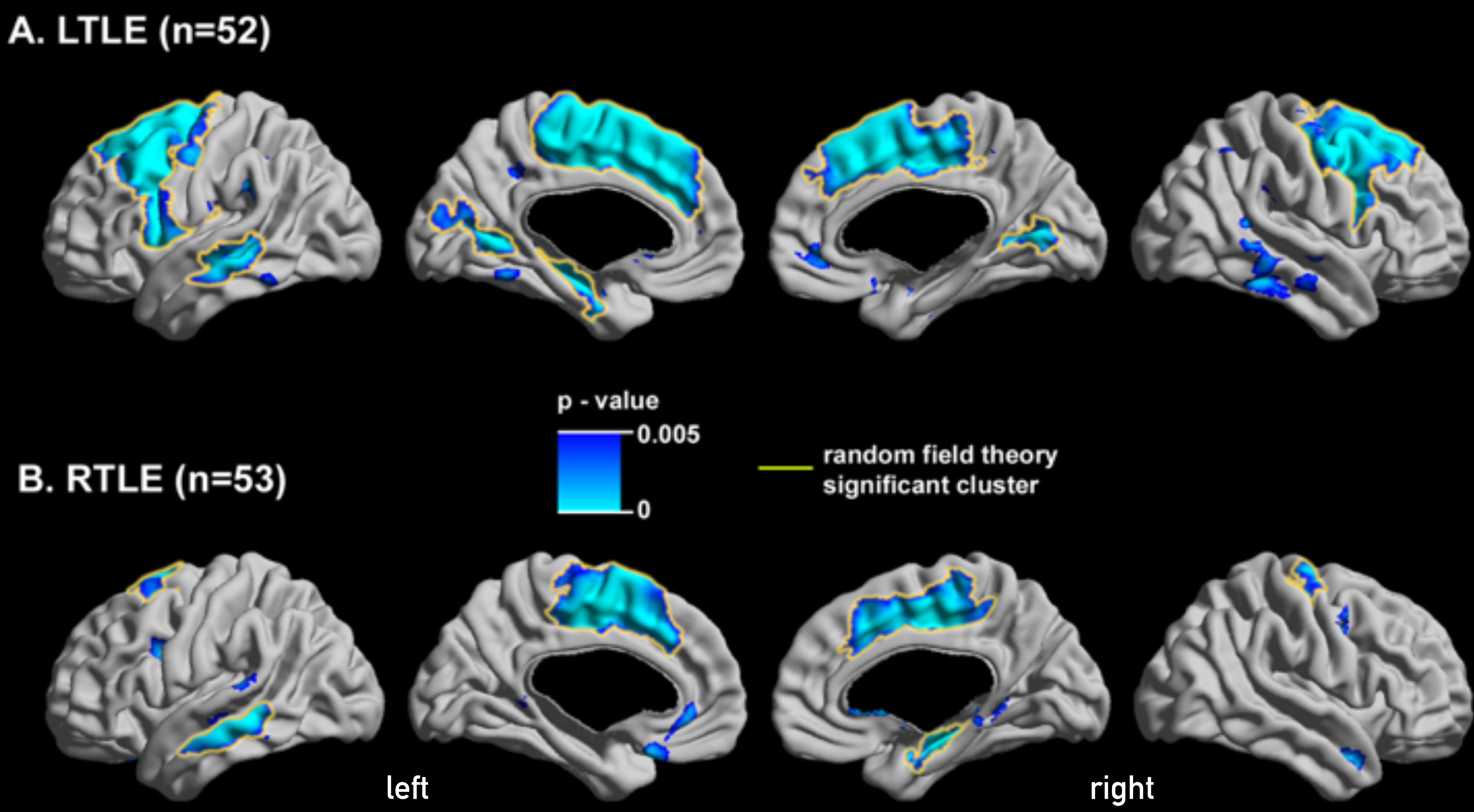


TLE

- temporal lobe epilepsy (TLE) most common drug-resistant epilepsy in adults
- seizures originate in TL, pathology often shows mesiotemporal sclerosis (MTS)
- hippocampal atrophy on MRI marker of MTS, lateralizes focus in 70%
- HA diagnosis: better chances of seizure-free surgical outcome

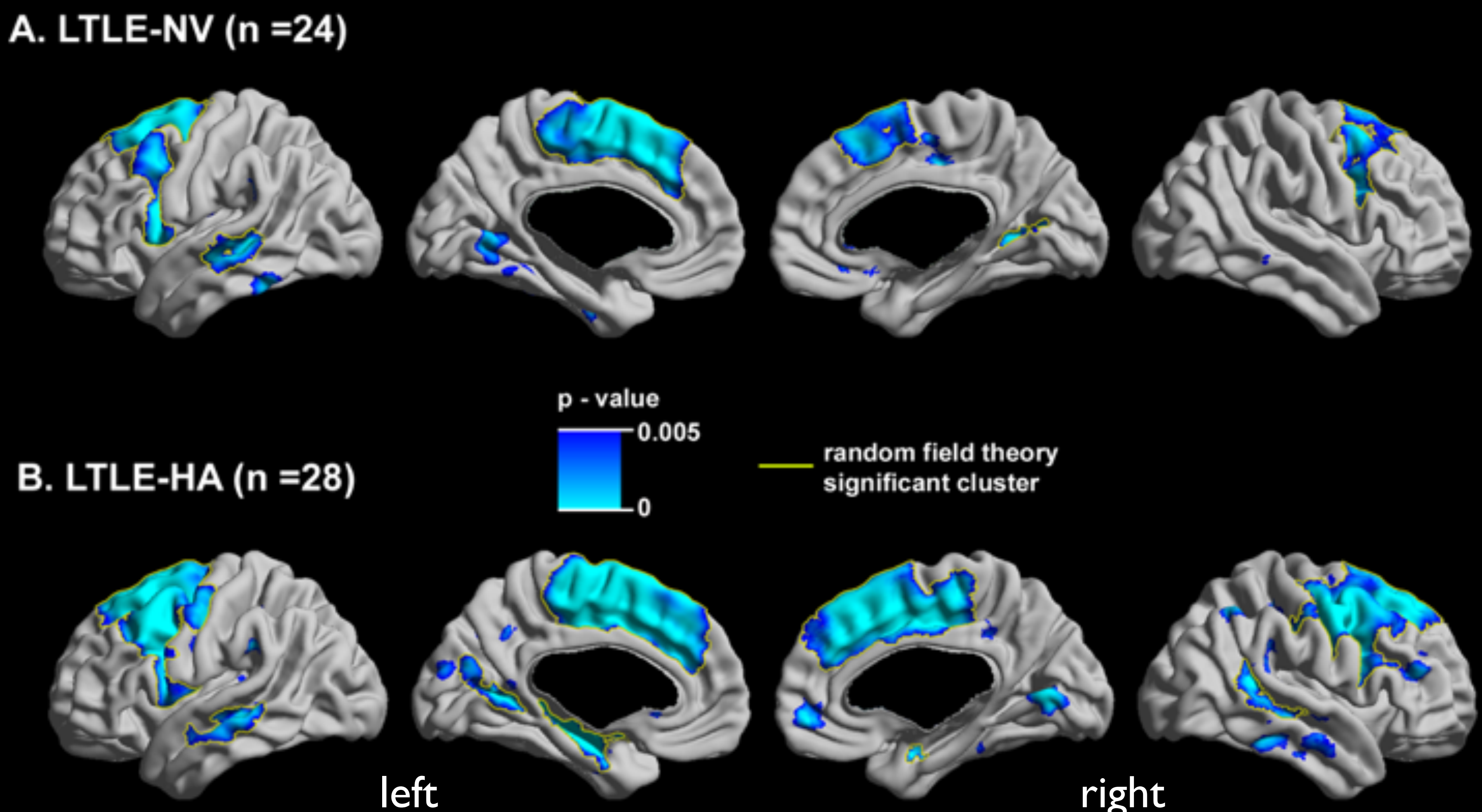
- long-term seizure-freedom in 50-80% of patients
- outcome prediction challenging
- outcome likely relates to brain damage outside mesiotemporal lobe

cortical thinning in TLE



Bernhardt et al. (2010) Neurology

influence of hippocampal atrophy



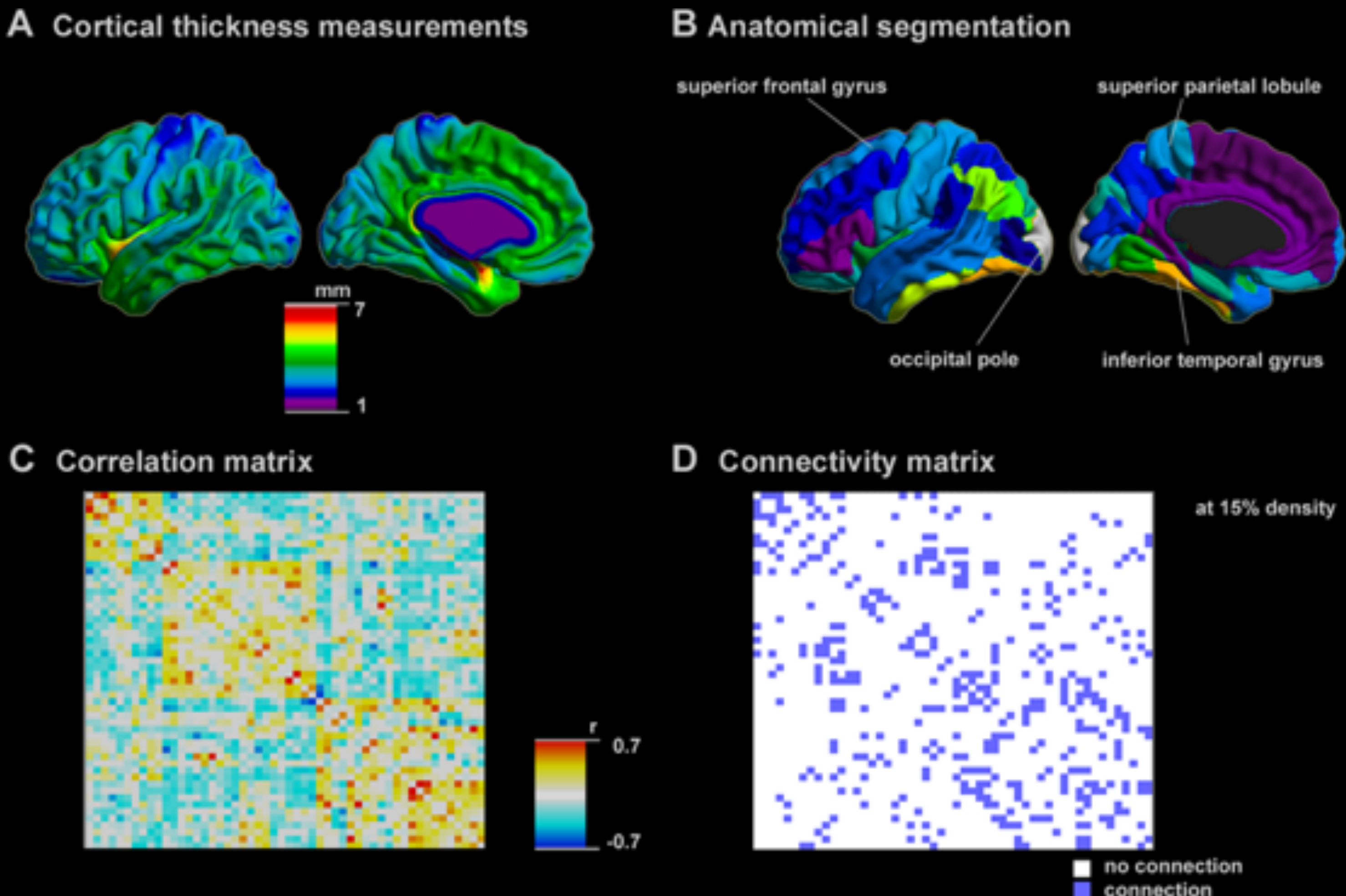
Bernhardt et al. (2010) Neurology

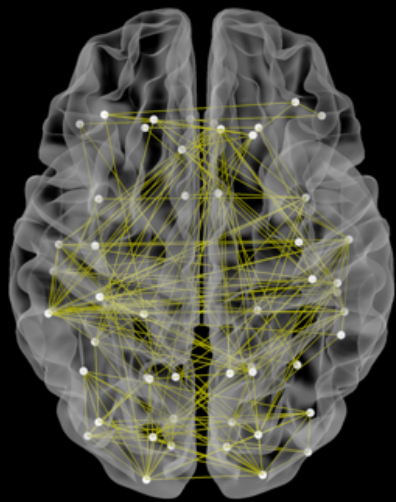
interim conclusion 1

- cortical thinning in fronto-central and lateral temporal neocortex
- seen across the spectrum of TLE
- seen at 1.5T, 3T, with CLASP and FreeSurfer (McDonald 2008 Epilepsia; Mueller 2010 NIMG)
- consistent with pathological examination (Blanc 2011 Epilepsia)

- widespread pathology indicative of system-level network alterations
- motivation for graph theoretical network analysis

addressing system pathology in TLE



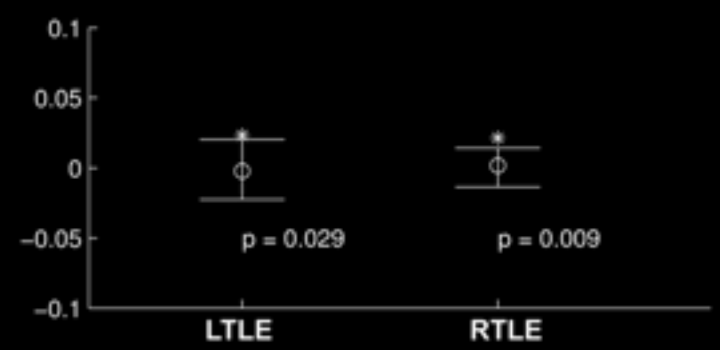


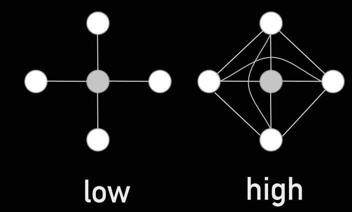
n=63 LTLE, 59 RTLE, 47 controls

Bernhardt et al. (2011) CerCor

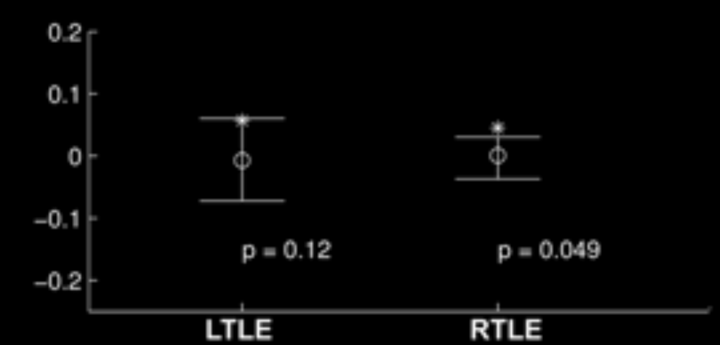
network regularization in TLE

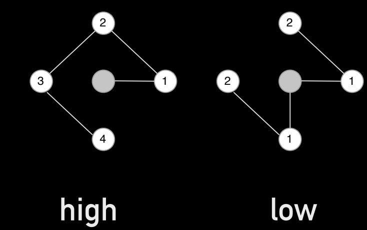
A Clustering coefficient (C)





B Path length (P)

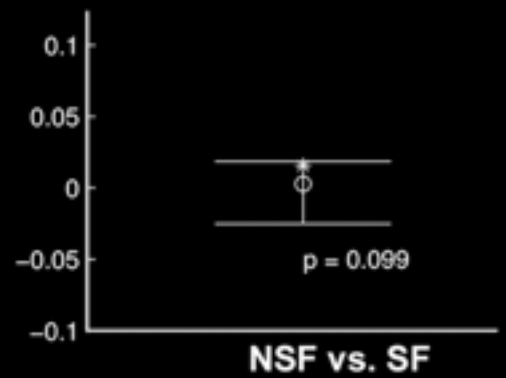


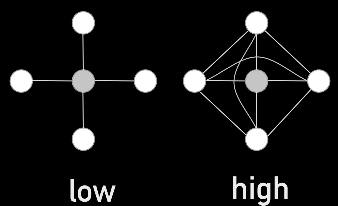


Bernhardt et al. (2011) CerCor

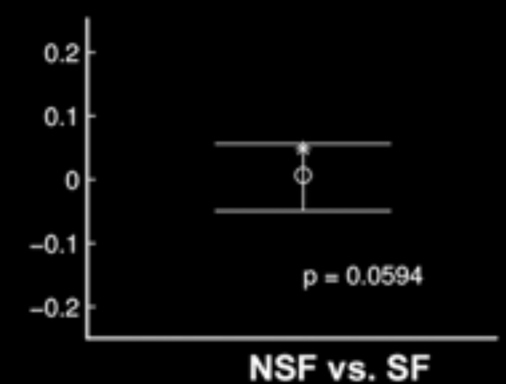
relationship to outcome

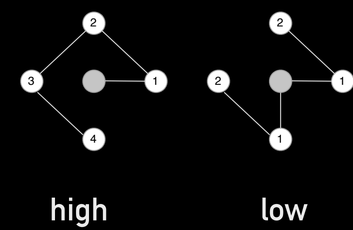
A Clustering coefficient (C)





B Path length (P)





50 SF versus 40 NSF

Bernhardt et al. (2011) CerCor

interim conclusion 2

TLE system disorder

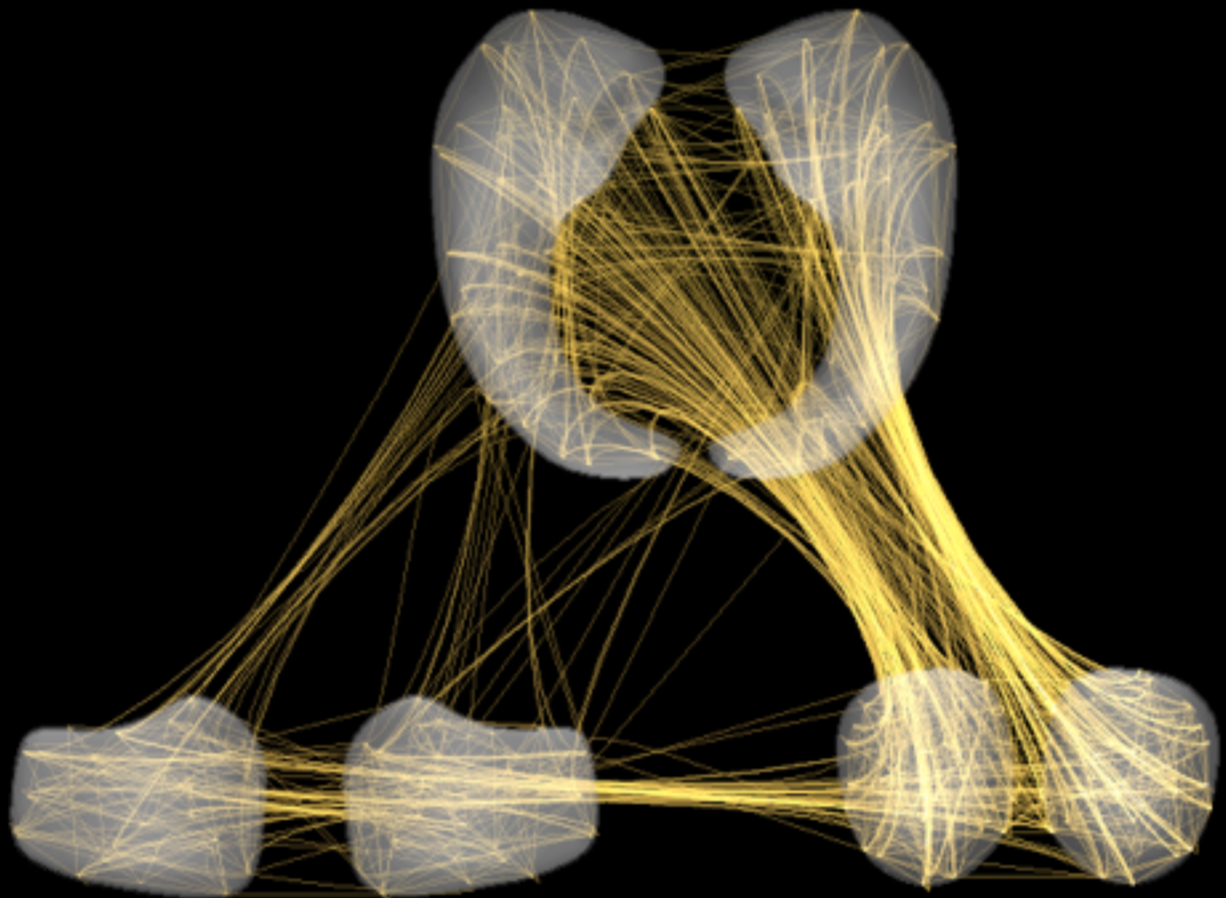
- cortico-cortical network regularization (↑P, ↑C)
- degree of network pathology relates to outcome

↑P

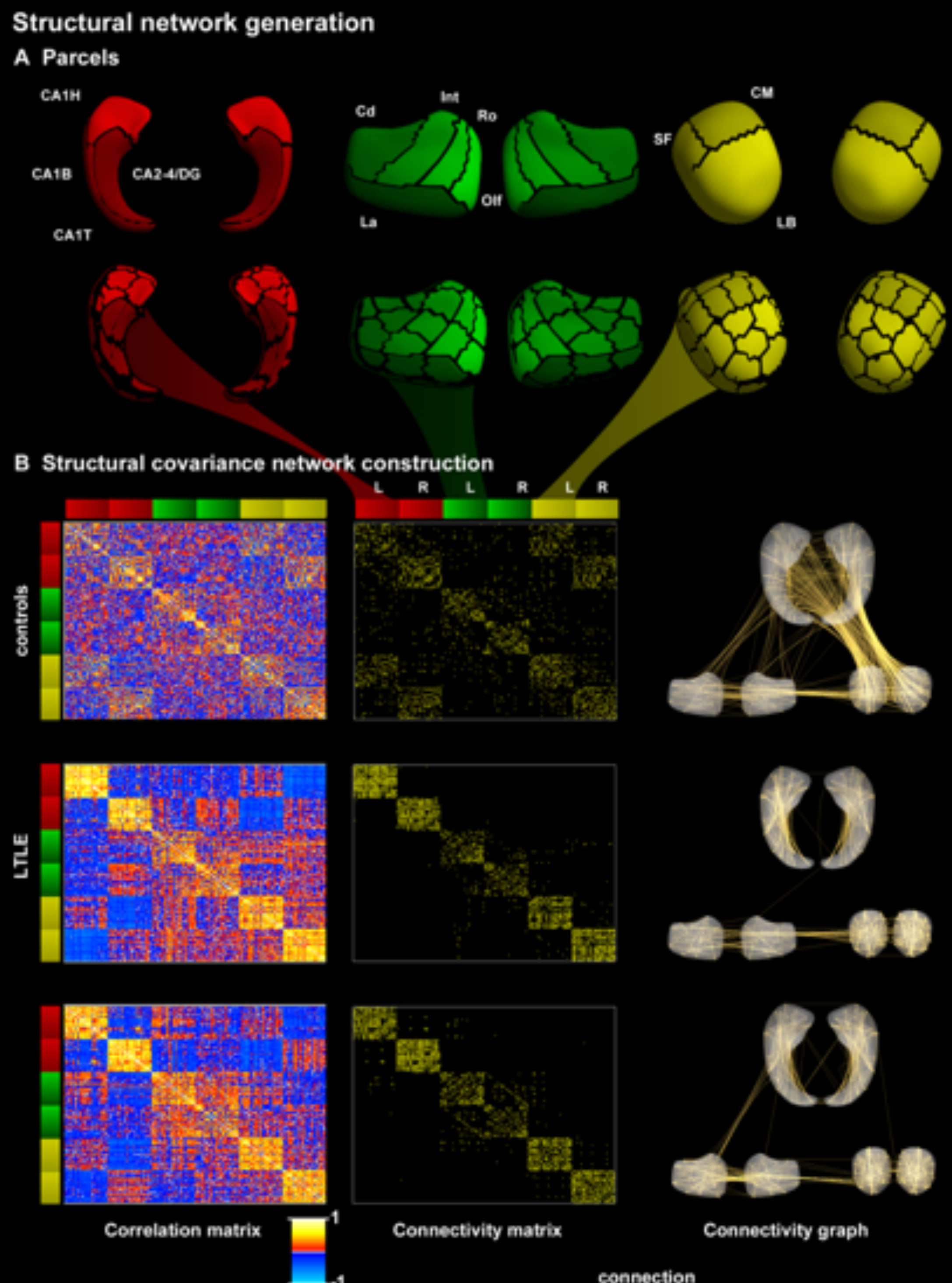
- likely indicative of disruptions in cortico-cortical connections
  (Concha 2005 Annals Neurology; Focke 2008 NIMG)
- may relate to cognitive impairments in TLE

↑C

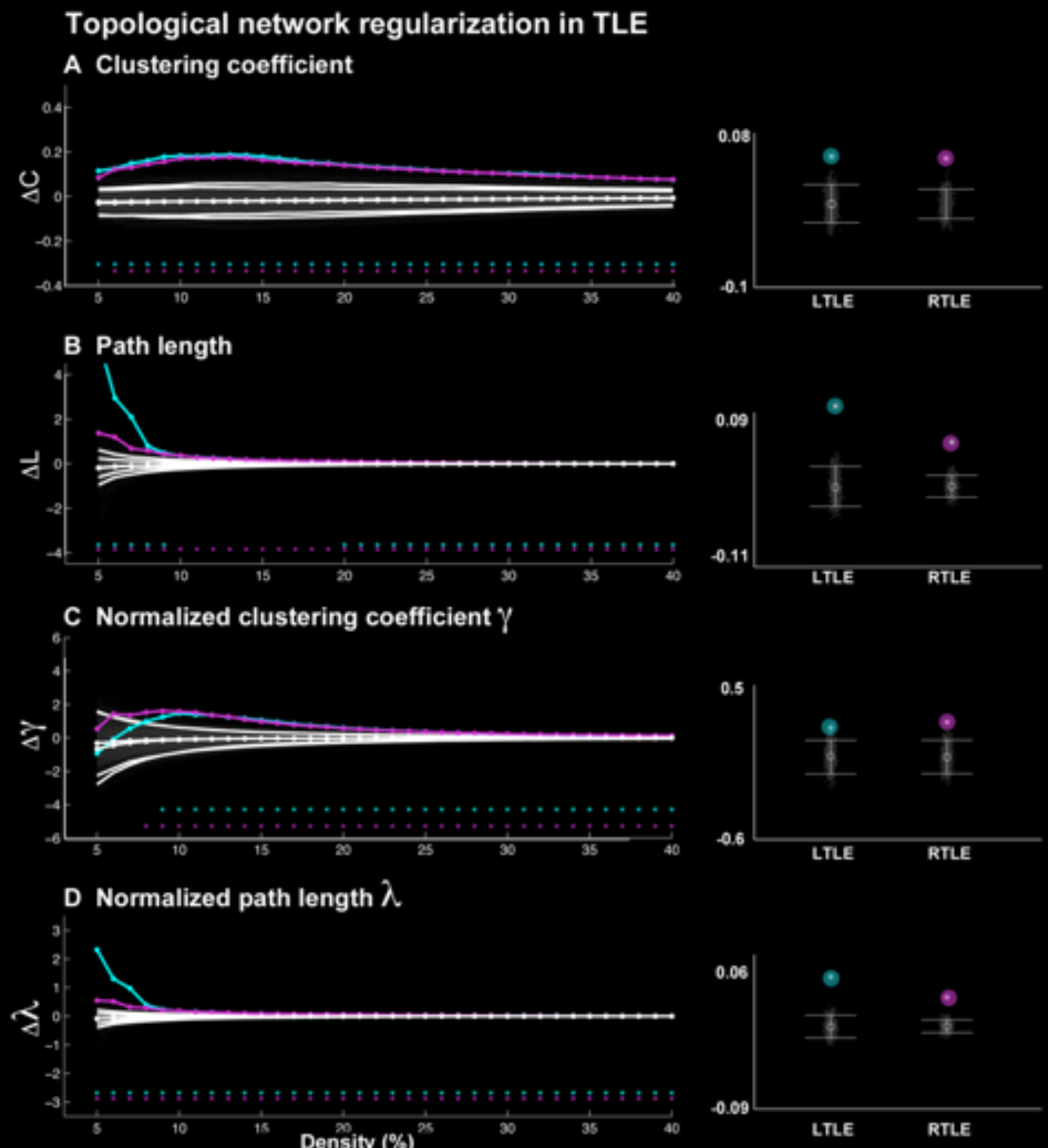
- increased pathological coupling in affected subnetworks
- possibly indicative of shared sensitivity to insults



Sebastien Dery, NeuroSPEED

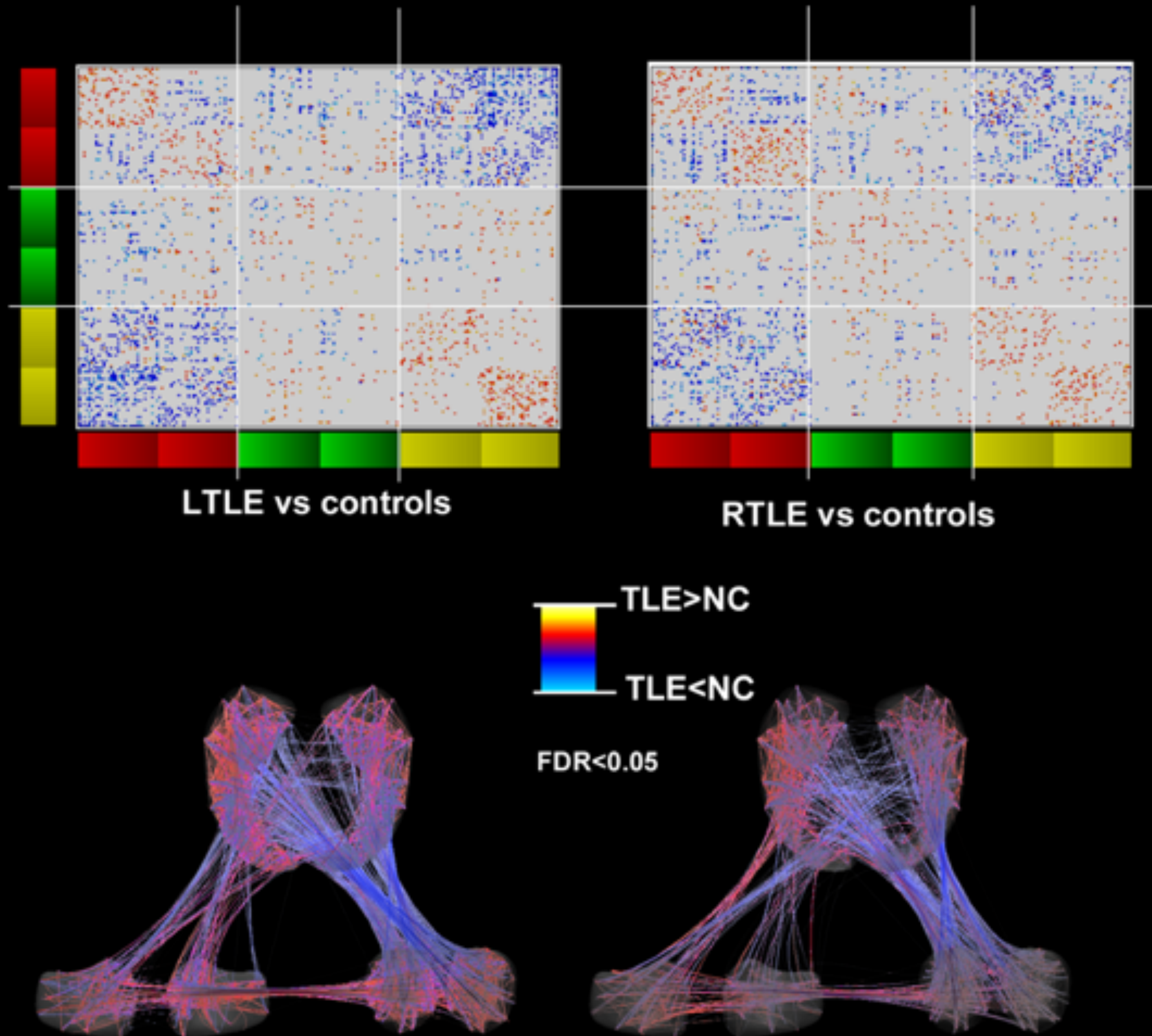


Bernhardt, et al. (submitted)



Bernhardt, et al. (submitted)

Low-Level network differences



Bernhardt, et al. (submitted)

interim conclusion 3

- subregional network regularization (↑P and ↑C)
  - ↑ within-structure covariance (possibly related to sprouting)
  - ↓ between-structure covariance (possibly related to disconnection)
  - ↑P in HA vs NV

- however: ↑P in SF vs NSF, controlling for HA diagnosis
  - Divergence between neocortical and mesiotemporal pathology wrt outcome

- network measures possible group-level biomarker

biomarkers

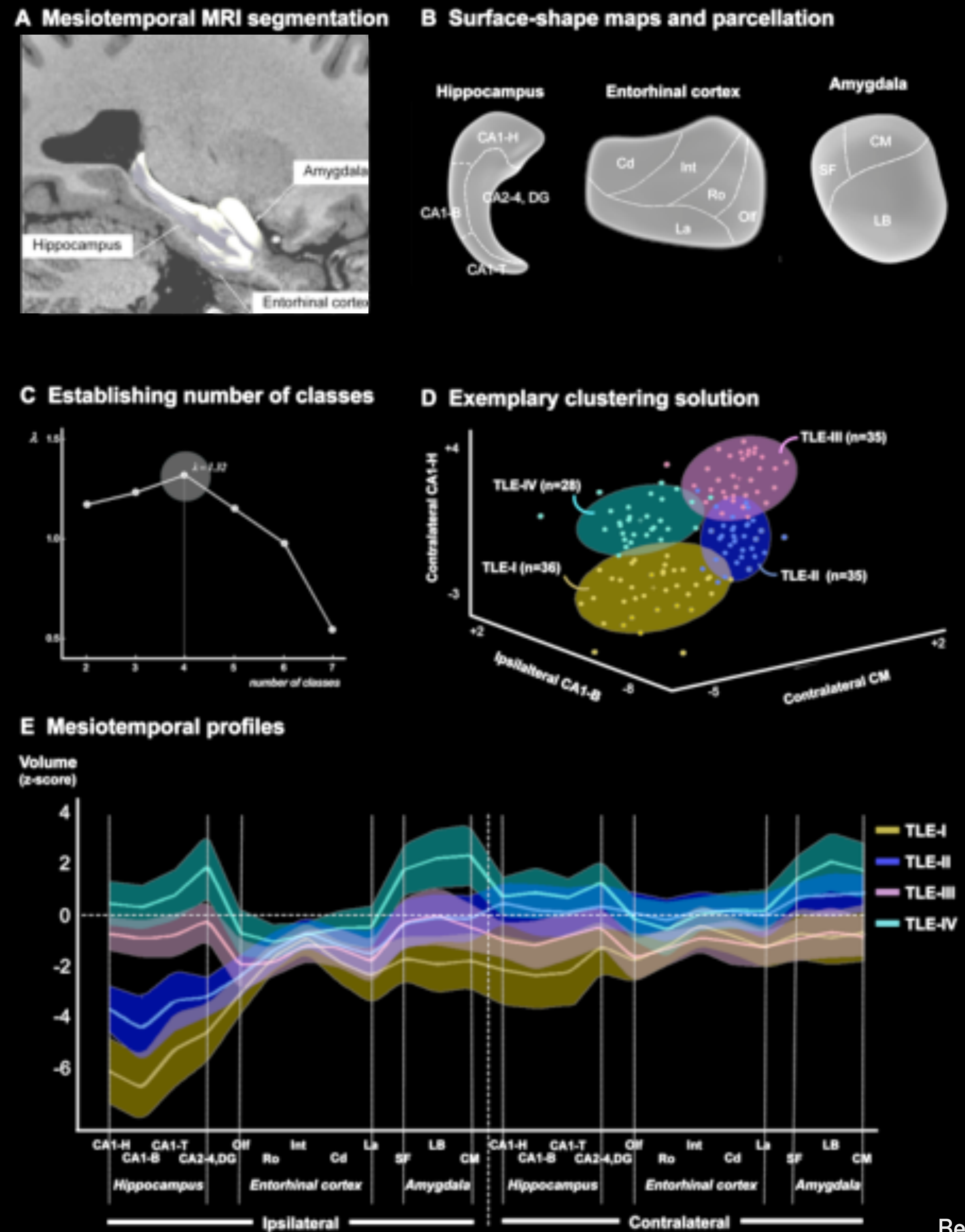
- prognostic biomarkers
  - may reveal clinical subpopulations of TLE

    goal: extend spectrum of TLE-HA vs TLE-NV

  - should ideally work on a patient-specific level

    goal: lateralize focus and predict outcome

- machine-learning lends appropriate tools for both goals
  - unsupervised clustering
  - supervised prediction



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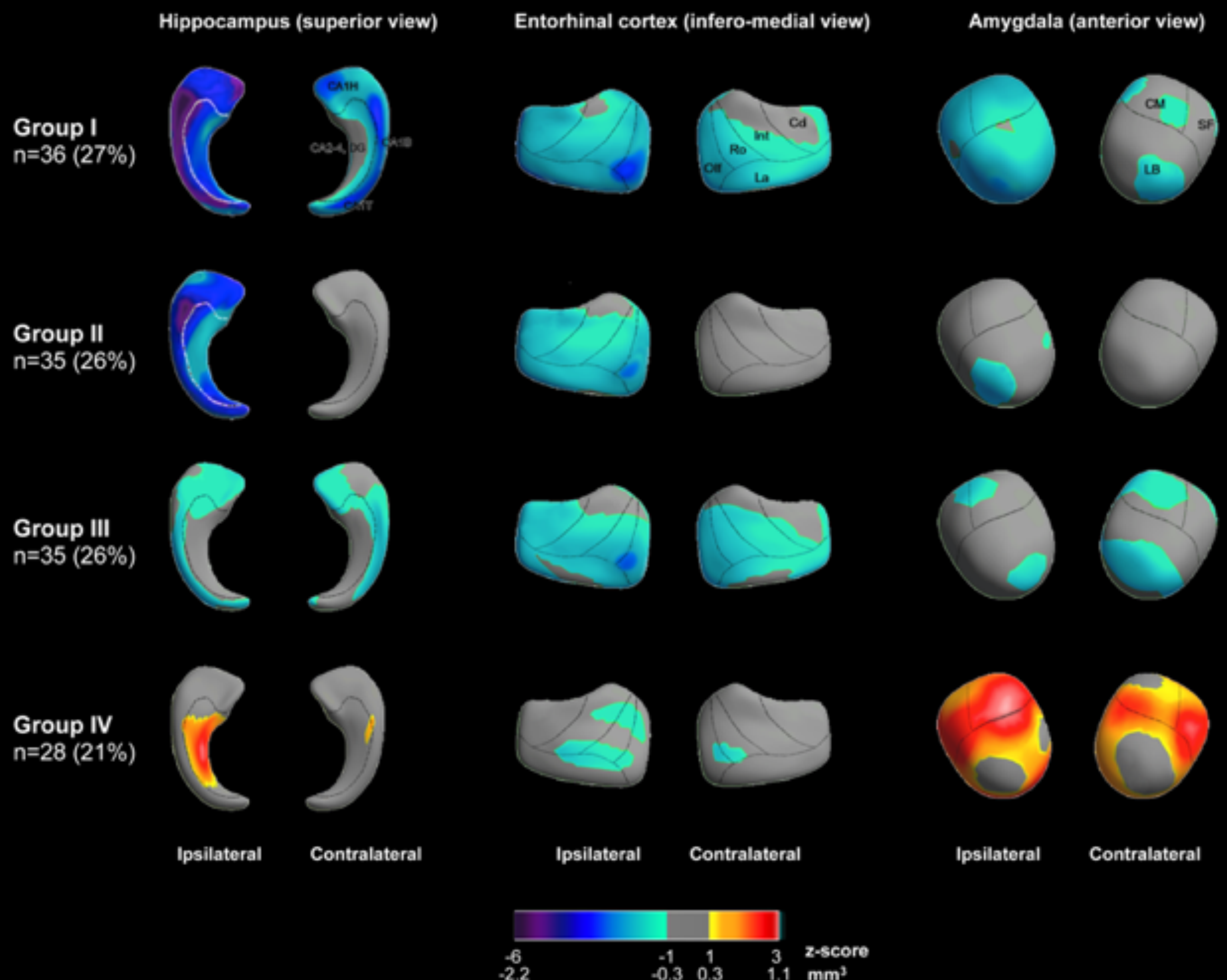
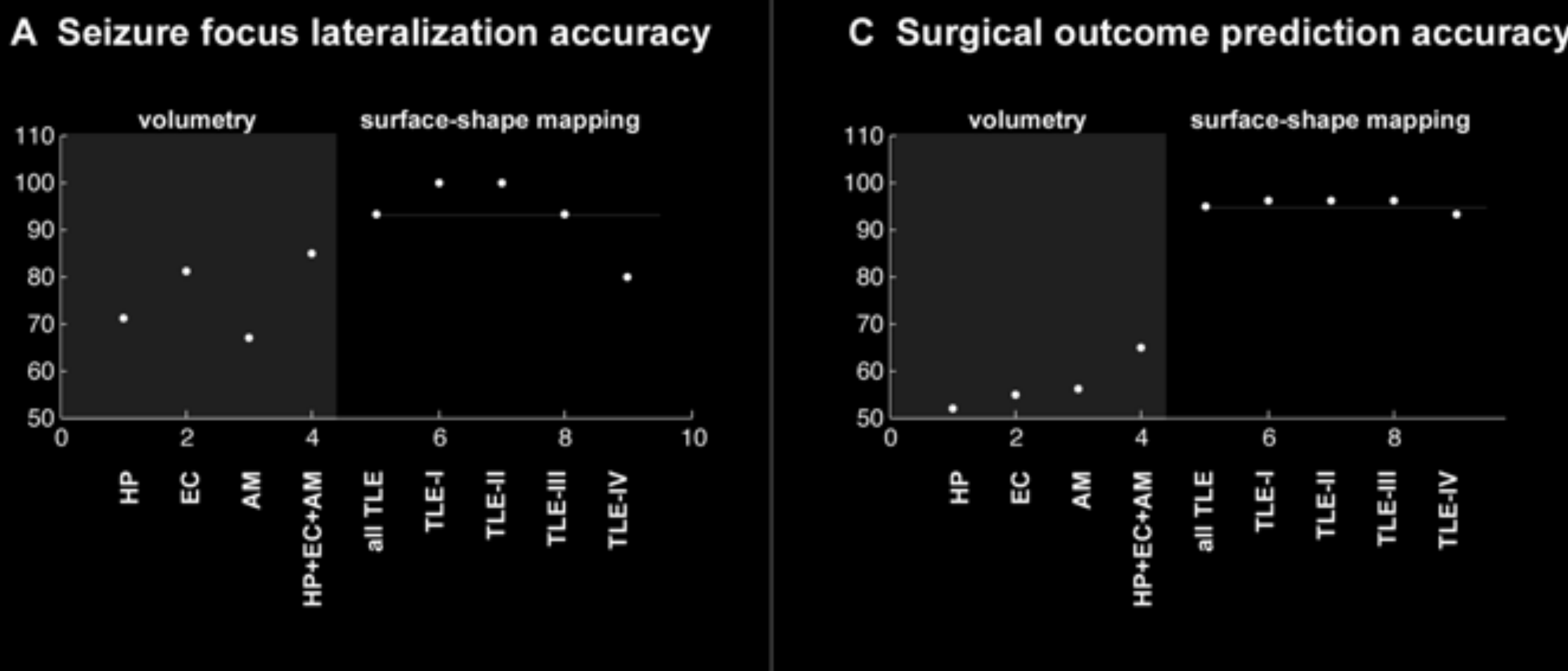


Bernhardt, et al. (submitted)

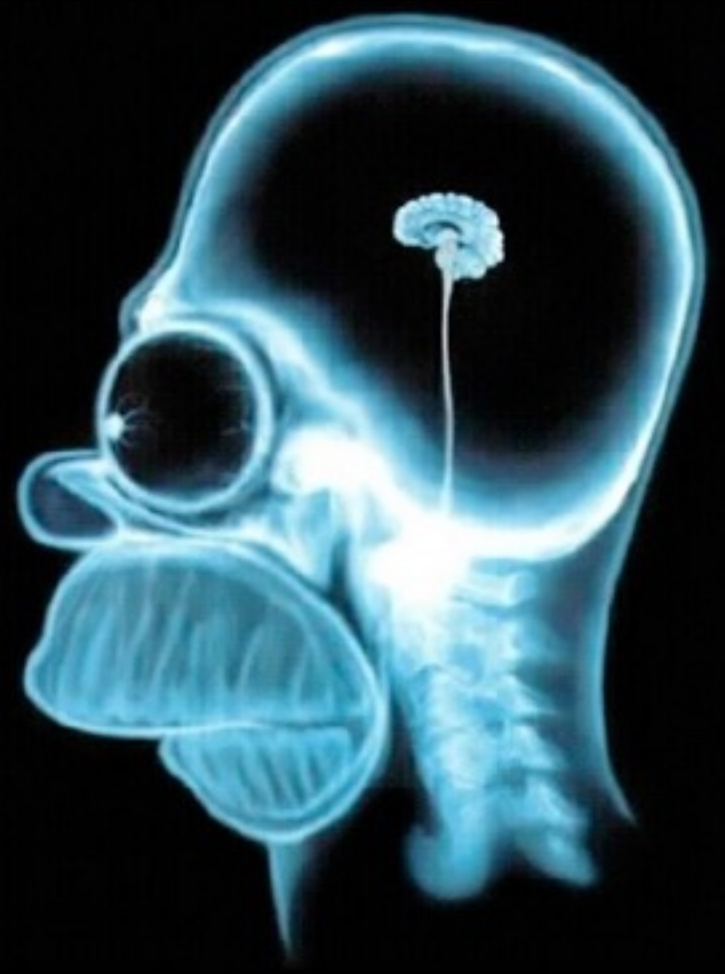
Clinical utility of mesiotemporal surface-shape mapping



Bernhardt, et al. (submitted)

conclusions

- MRI profiling provides nuanced characterization of TLE spectrum
  - consistent anterior entorhinal subfield atrophy
  - gradation of hippocampal-amygdala changes (atrophy >> hypertrophy)
- high level of clinical validity
  - 95% accurate prediction of outcome (conventional volumetry: 52%)
  - 93% accurate lateralization (conventional volumetry: 71%)
- promising biomarker for presurgical workup in drug-resistant TLE



overall summary

overall summary

structural MRI permits

- mapping substrates individual differences
- brain network analysis
- assessing brain pathology and biomarker discovery

complimentary tools can be used for meaningful analysis

- MRI volumetry
- surface-based methods
- structural MRI covariance analysis

merci!

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