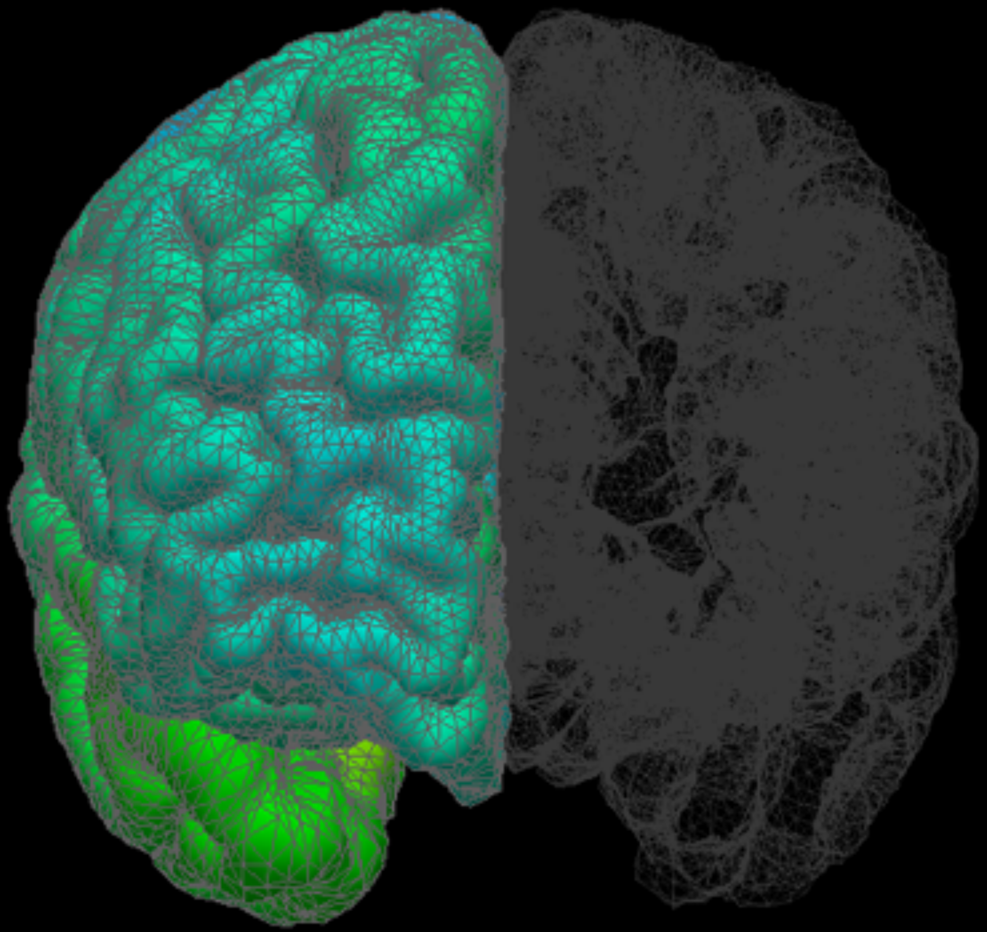

# Structural MRI analysis in the study of cognition

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NeuroImaging of Epilepsy Lab

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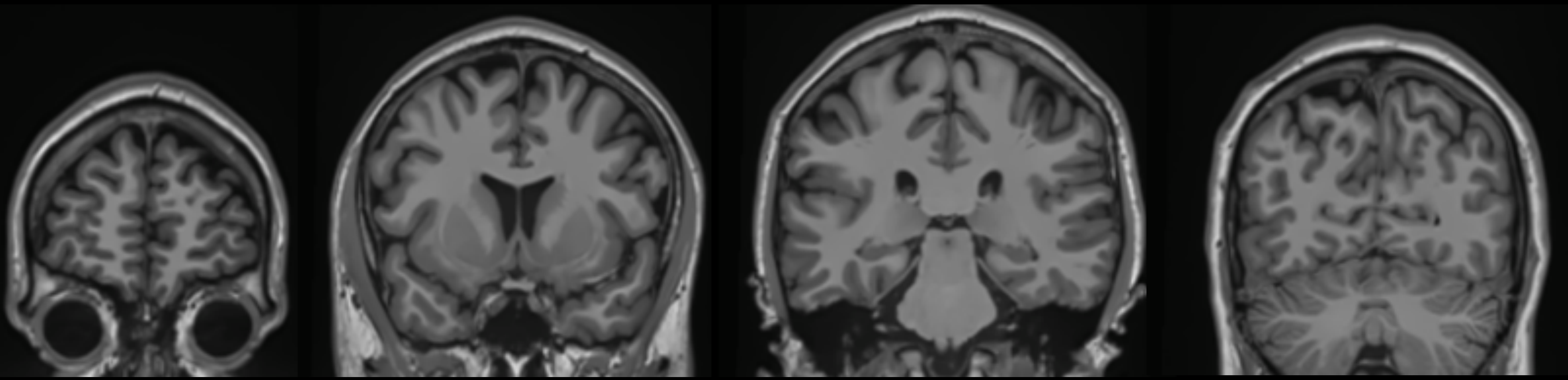
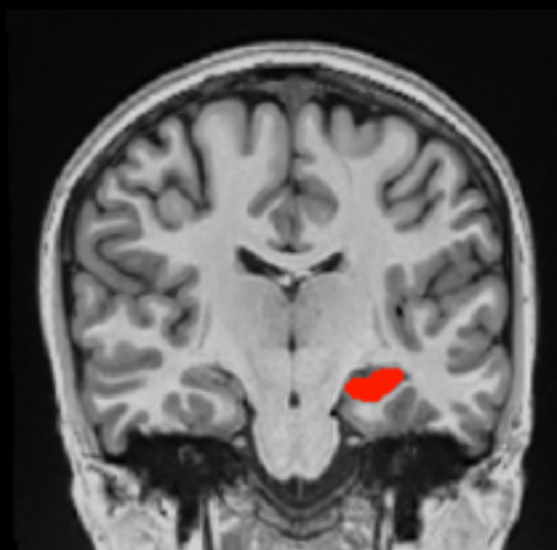
# structural MRI

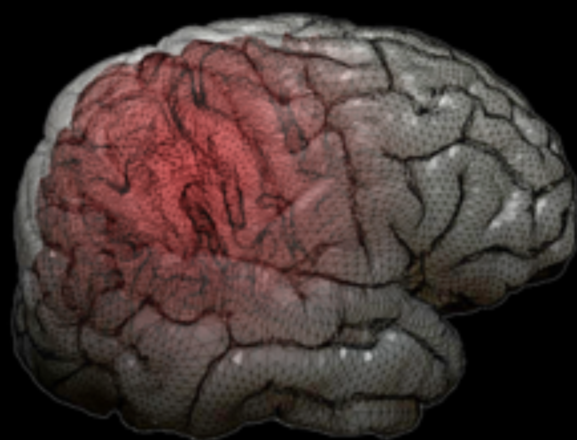


T1-weighted MRI

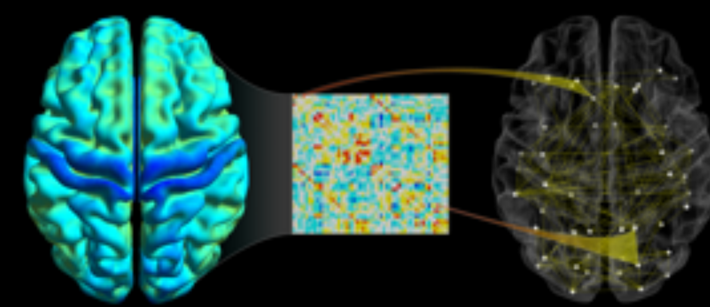
# methods



MRI volumetry

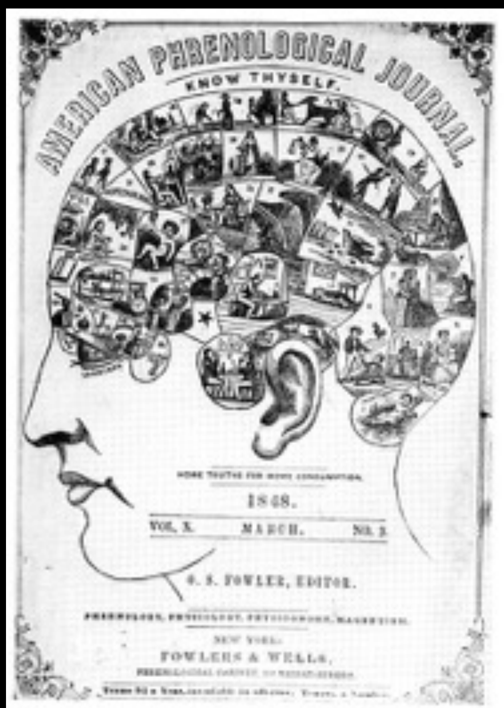


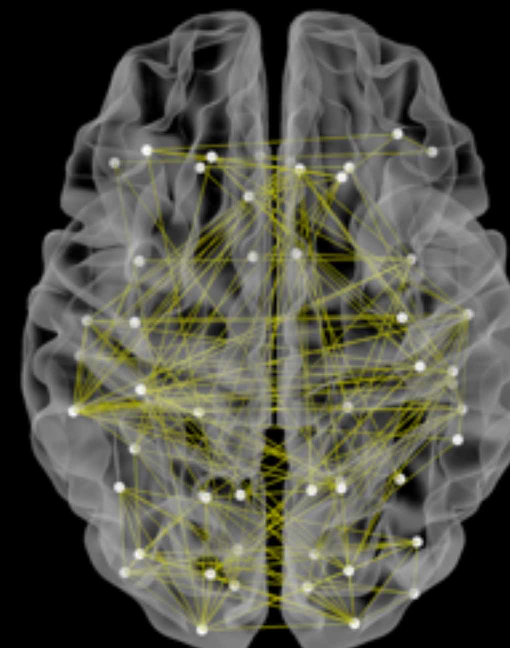
Surface-based analysis



Covariance mapping

# applications



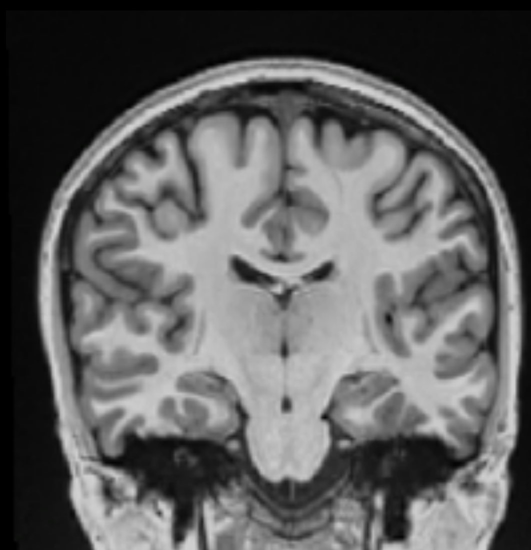



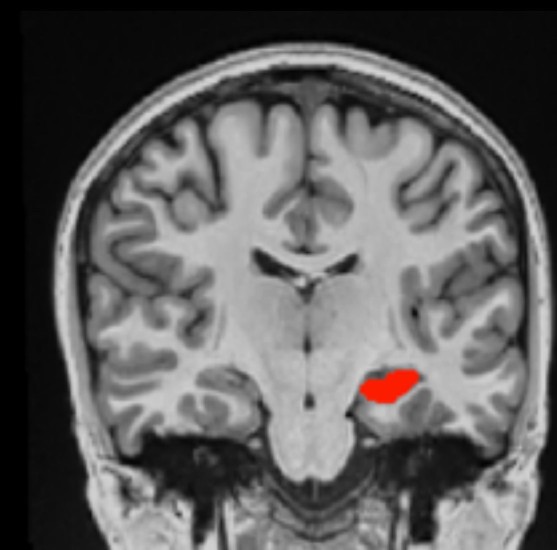
Individual differences

Brain disorders

Brain organization

# volumetry ‘pipeline’



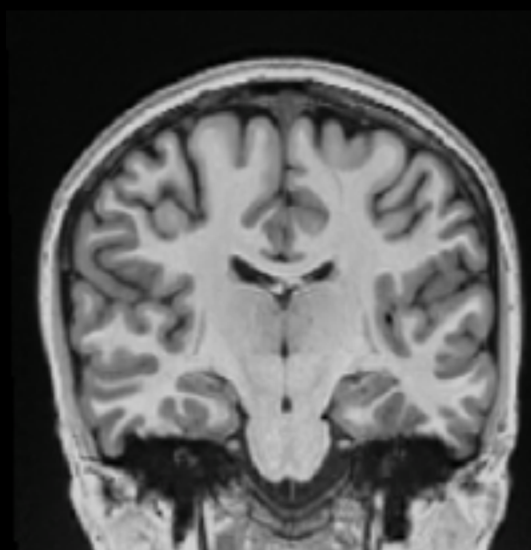



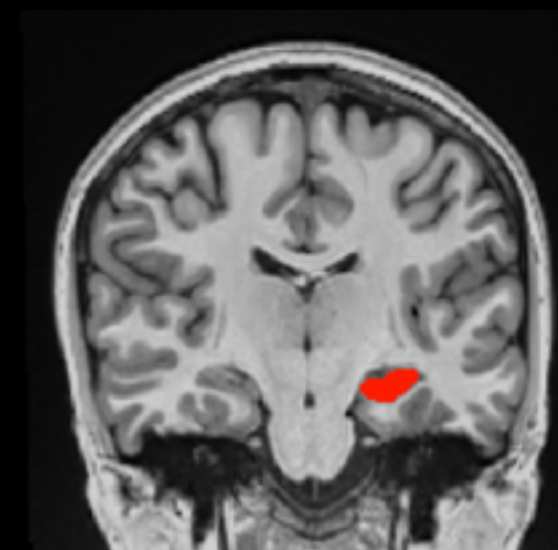
input

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

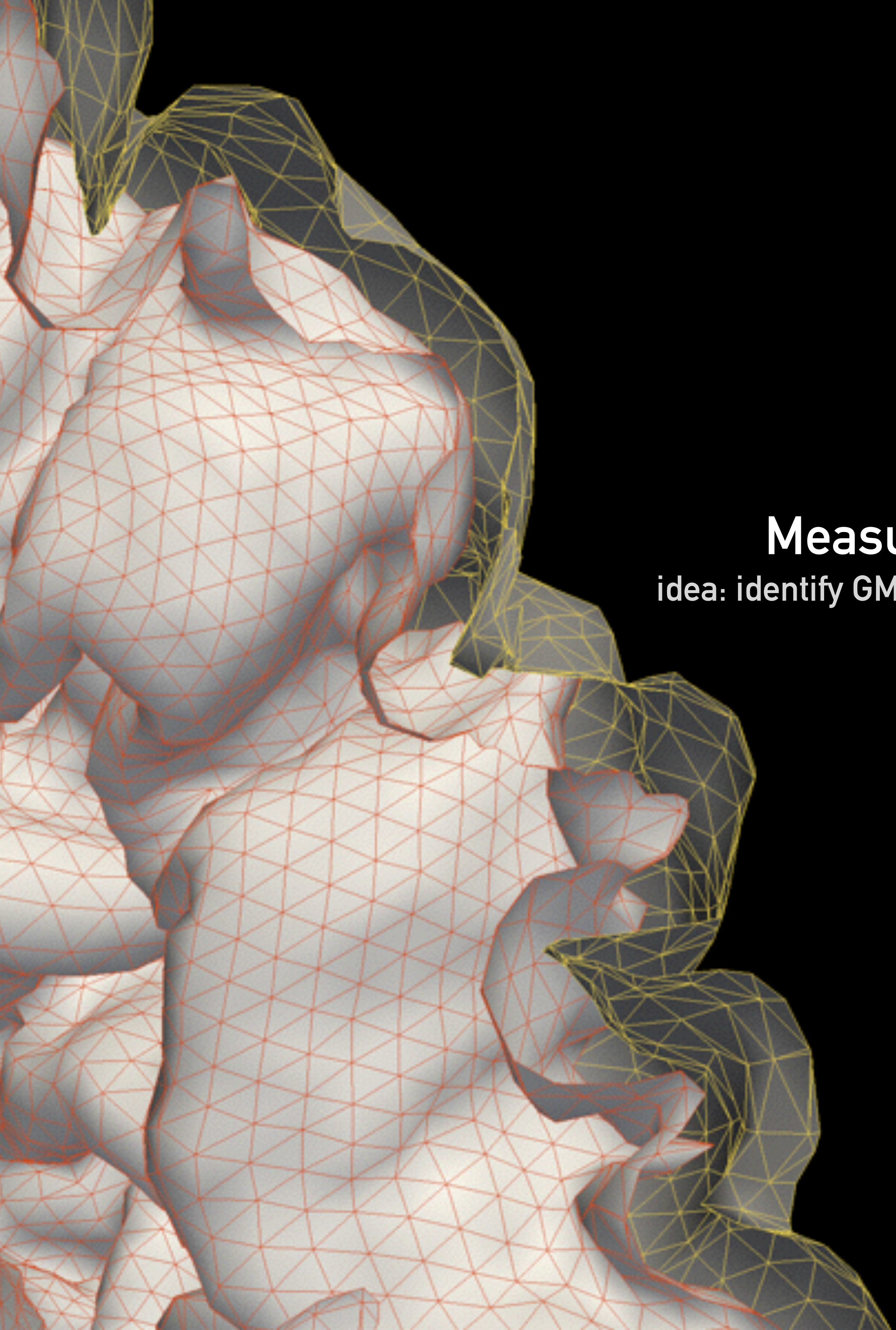
# MRI volumetry: pros and cons

Pros

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

Cons

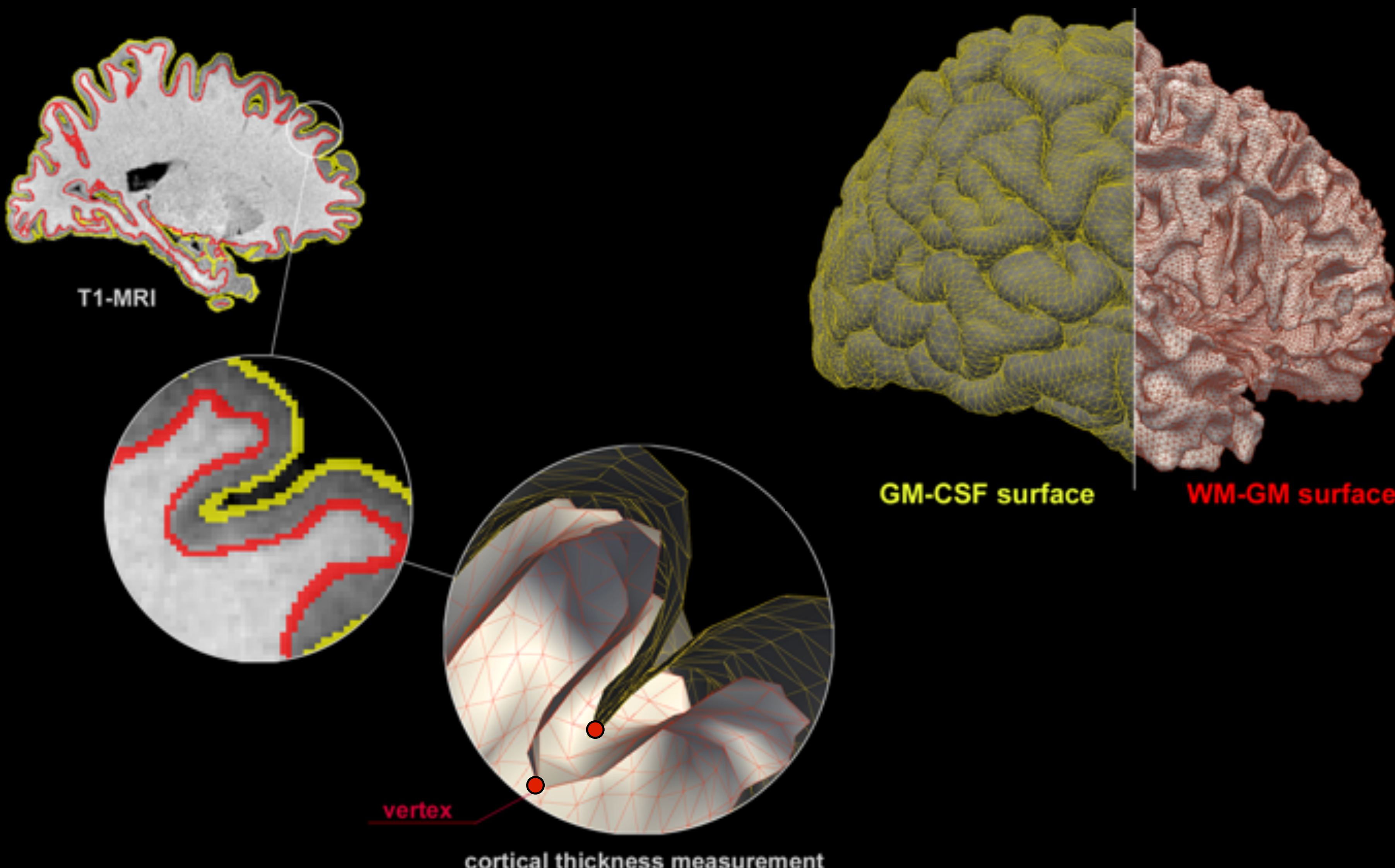
- labor-intensive manual segmentations are gold standard
- requires expert anatomical knowledge
- inter-rater, intra-rater variability, inter-protocol variability
- limited to individual anatomical regions



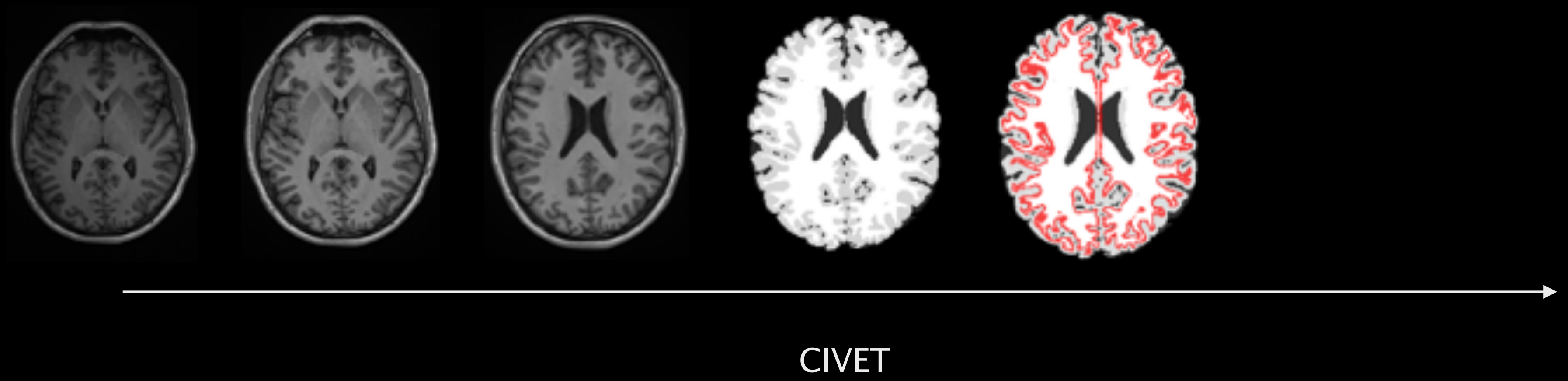
# Measuring cortical thickness on MRI

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

# MRI-based cortical thickness measurements



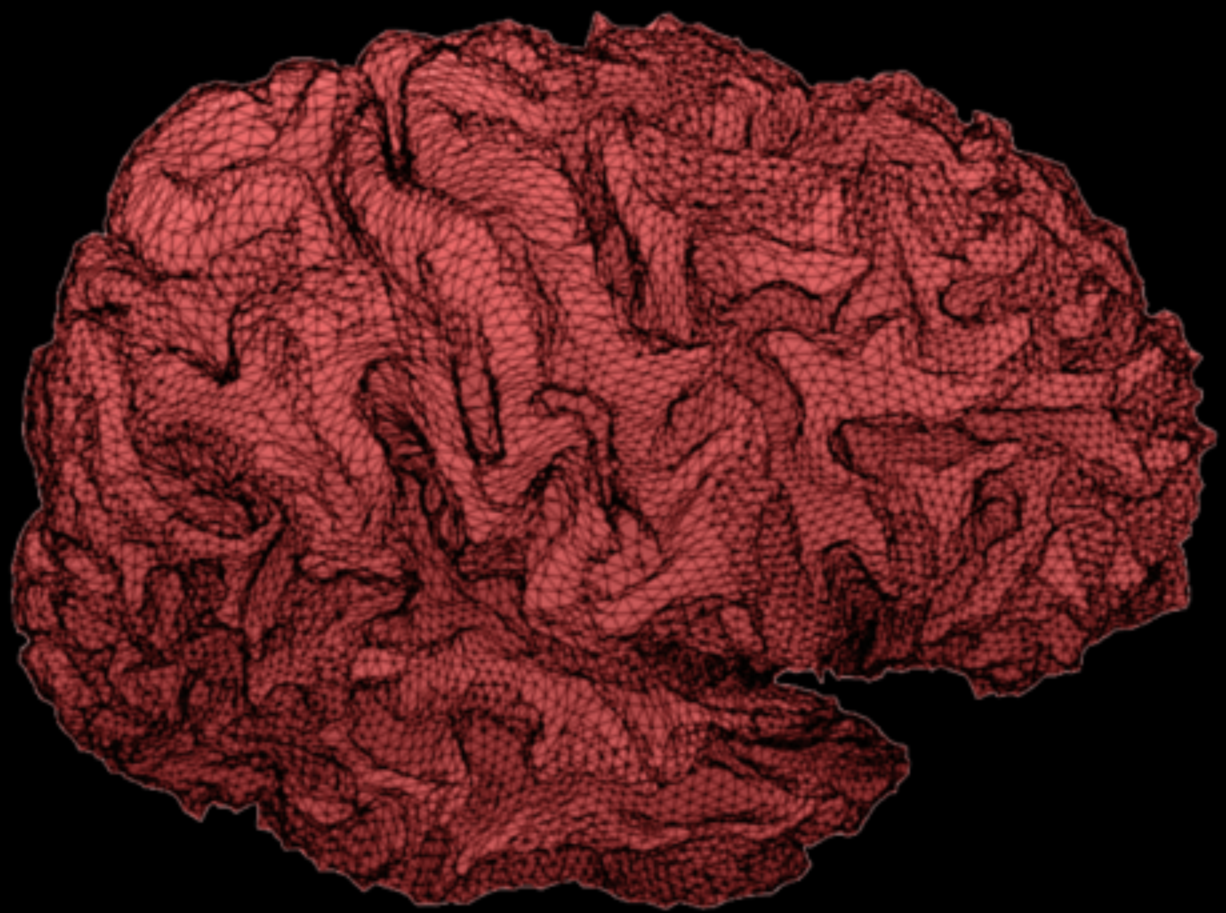
# some processing...



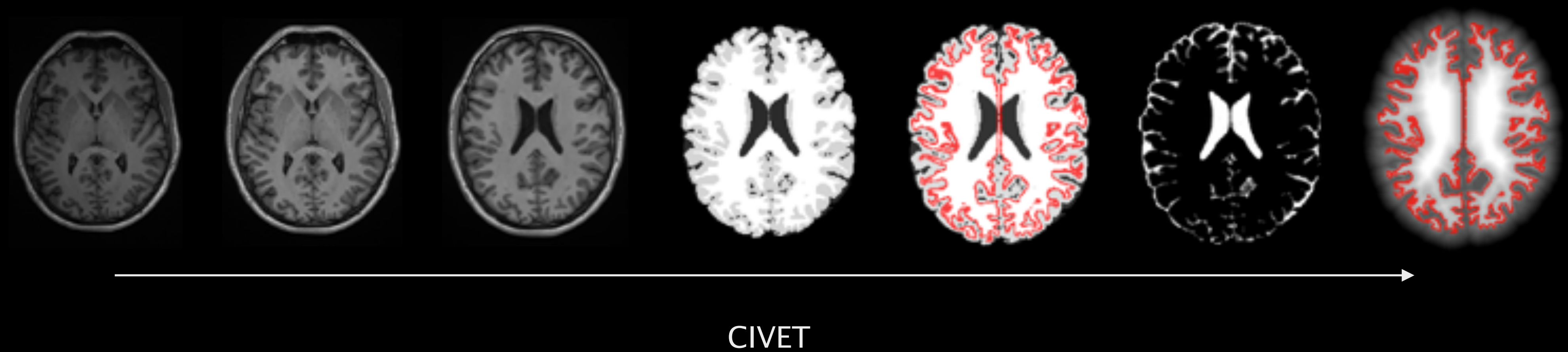

MacDonald et al. (2000) NeuroImage

Kim et al. (2005) NeuroImage

# WM surface



## further processing...

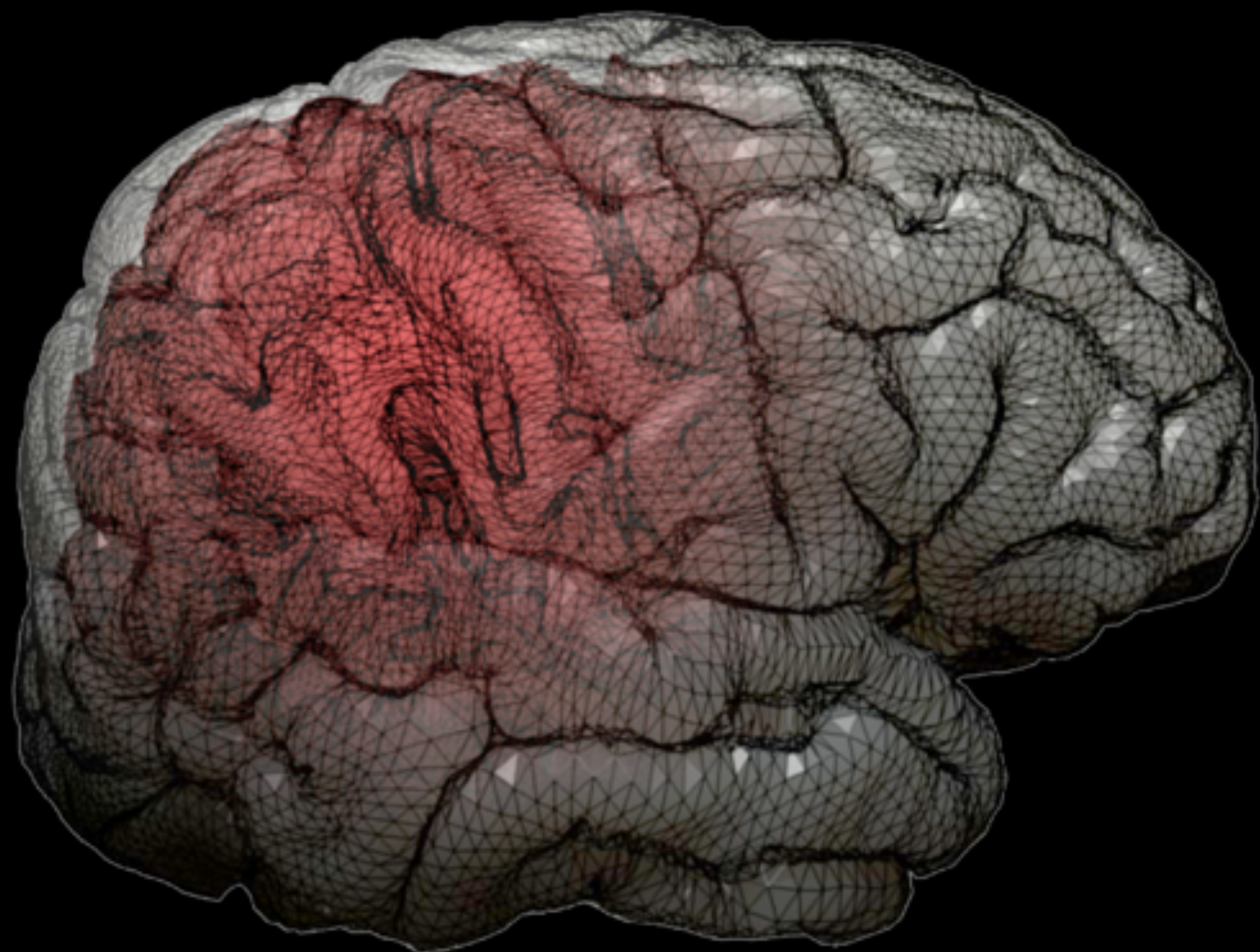



OMM: March 17

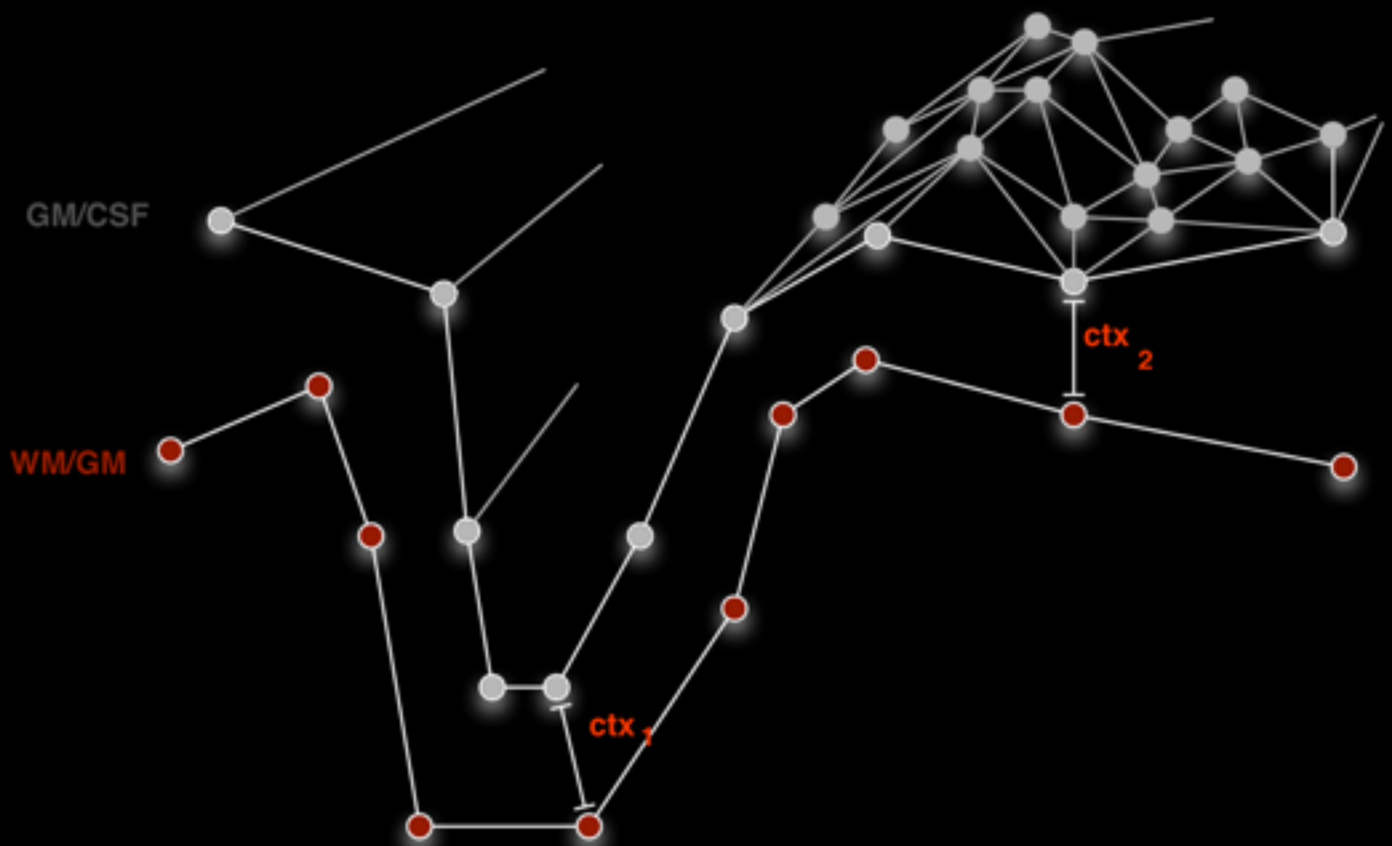
MacDonald et al. (2000) NeuroImage

Kim et al. (2005) NeuroImage

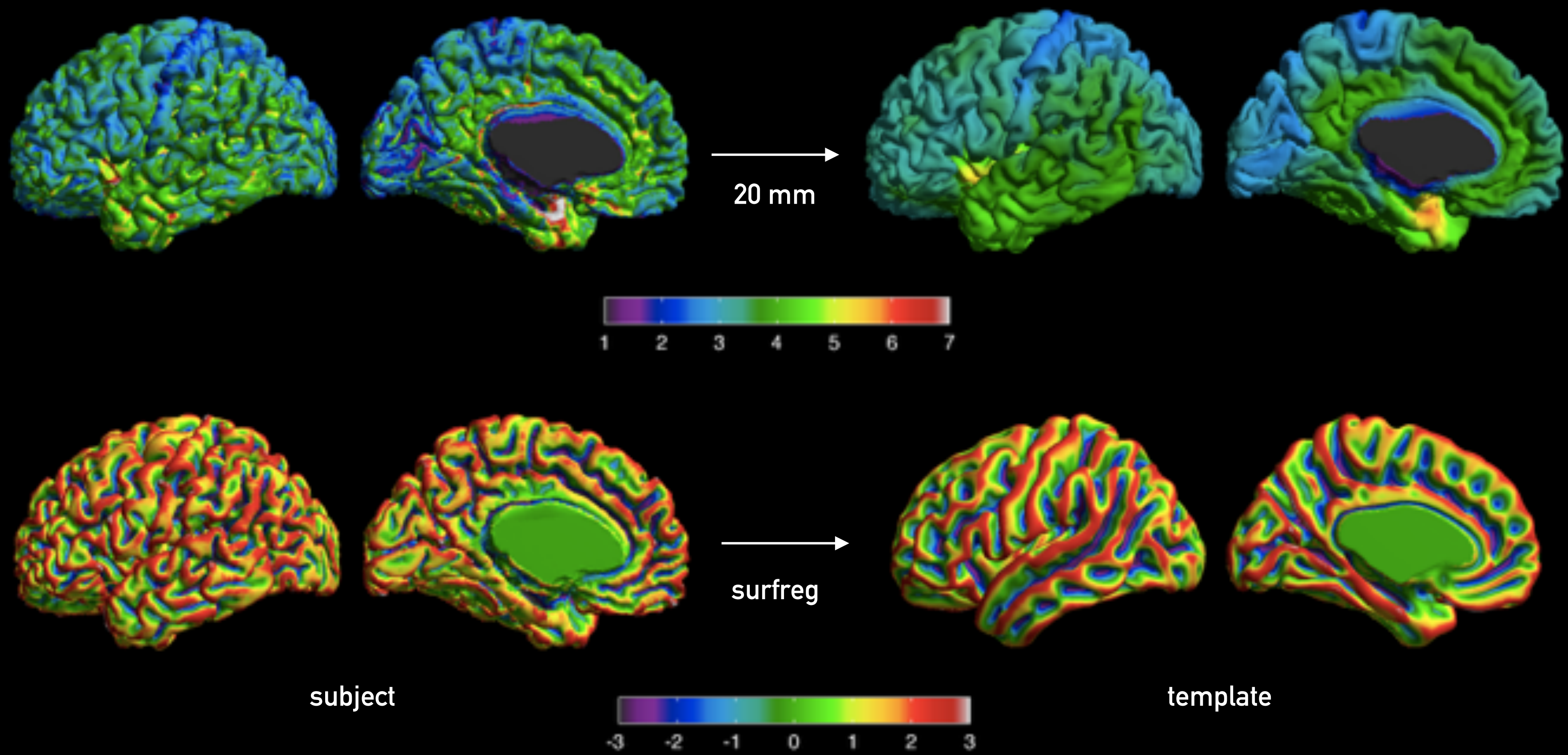
## GM surface



# measurement of cortical thickness



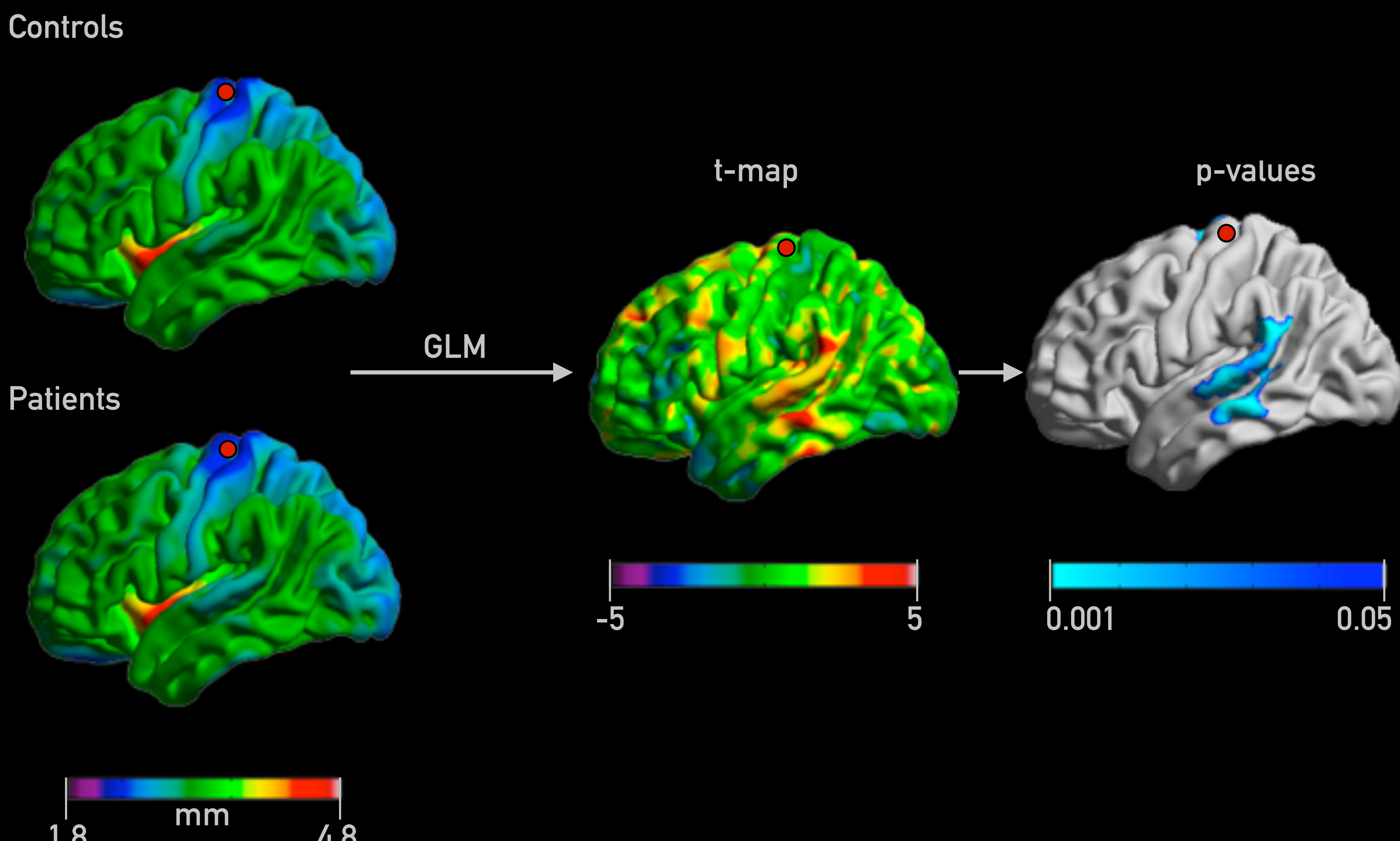
# surface-based processing




Chung et al. (2003) NeuroImage

Robbins et al. (2004) MedImaAnalysis

# statistical analysis using SurfStat




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

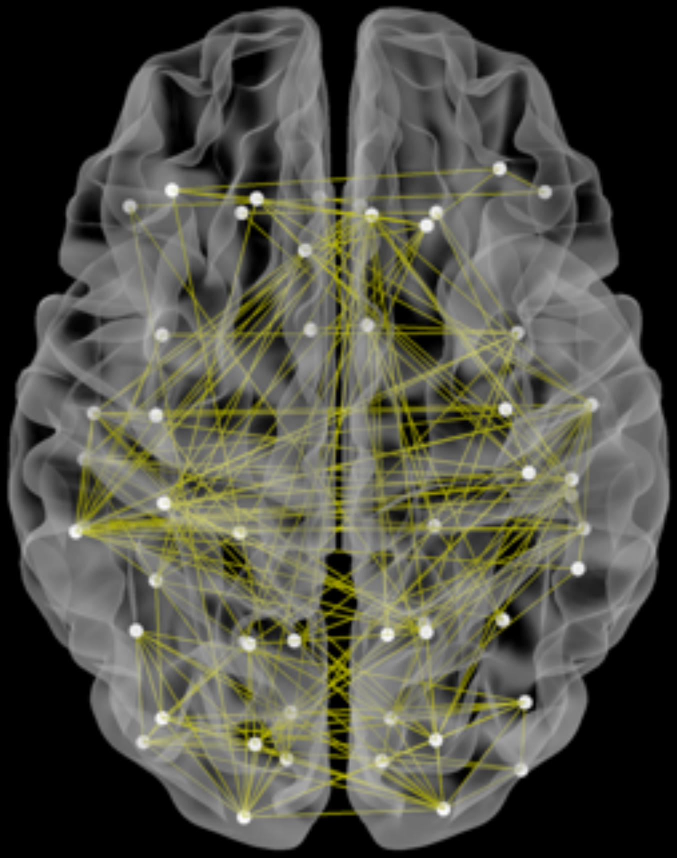
# cortical thickness: pros and cons

Pros

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

Cons

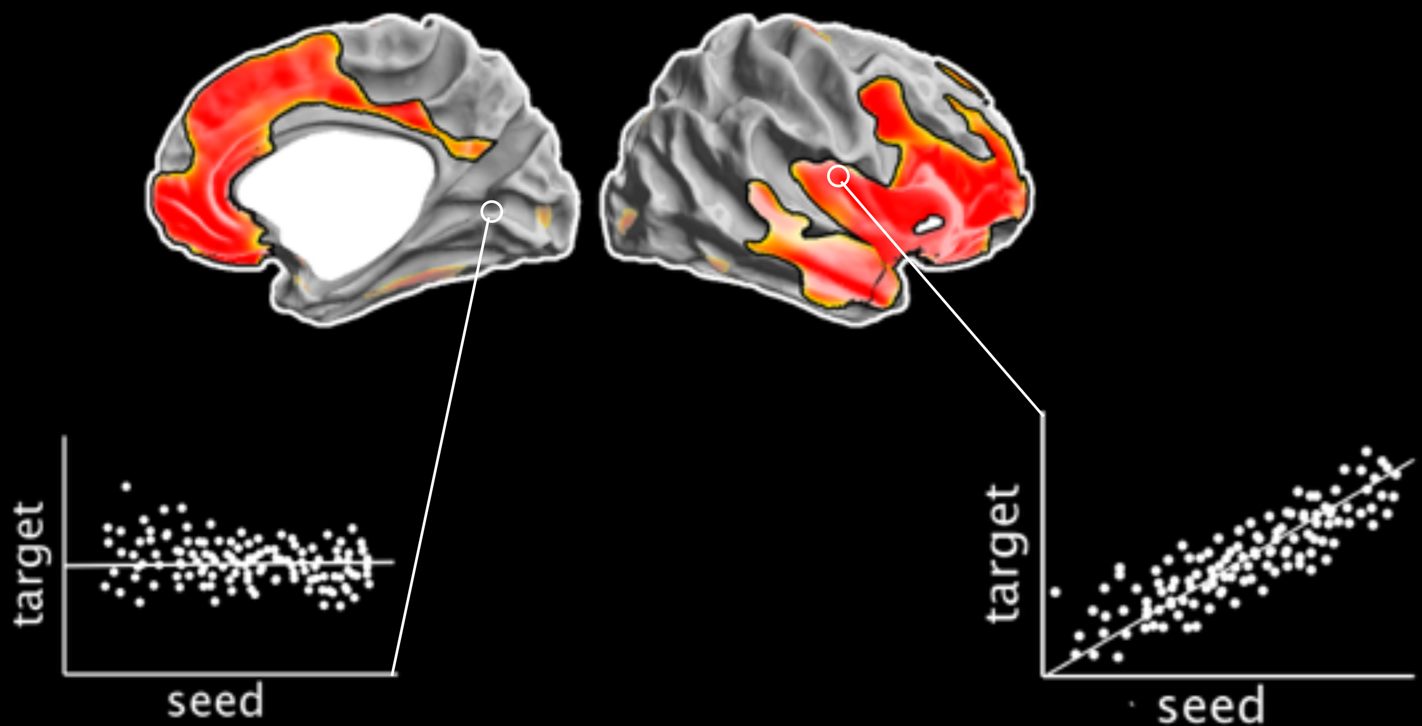
- heavy post-processing (4-25 hours/case)
- dependent on classification
- manual corrections often necessary
- limited to (neo)cortex



## Structural covariance network mapping

idea: connections = structural correlations between regions across subjects

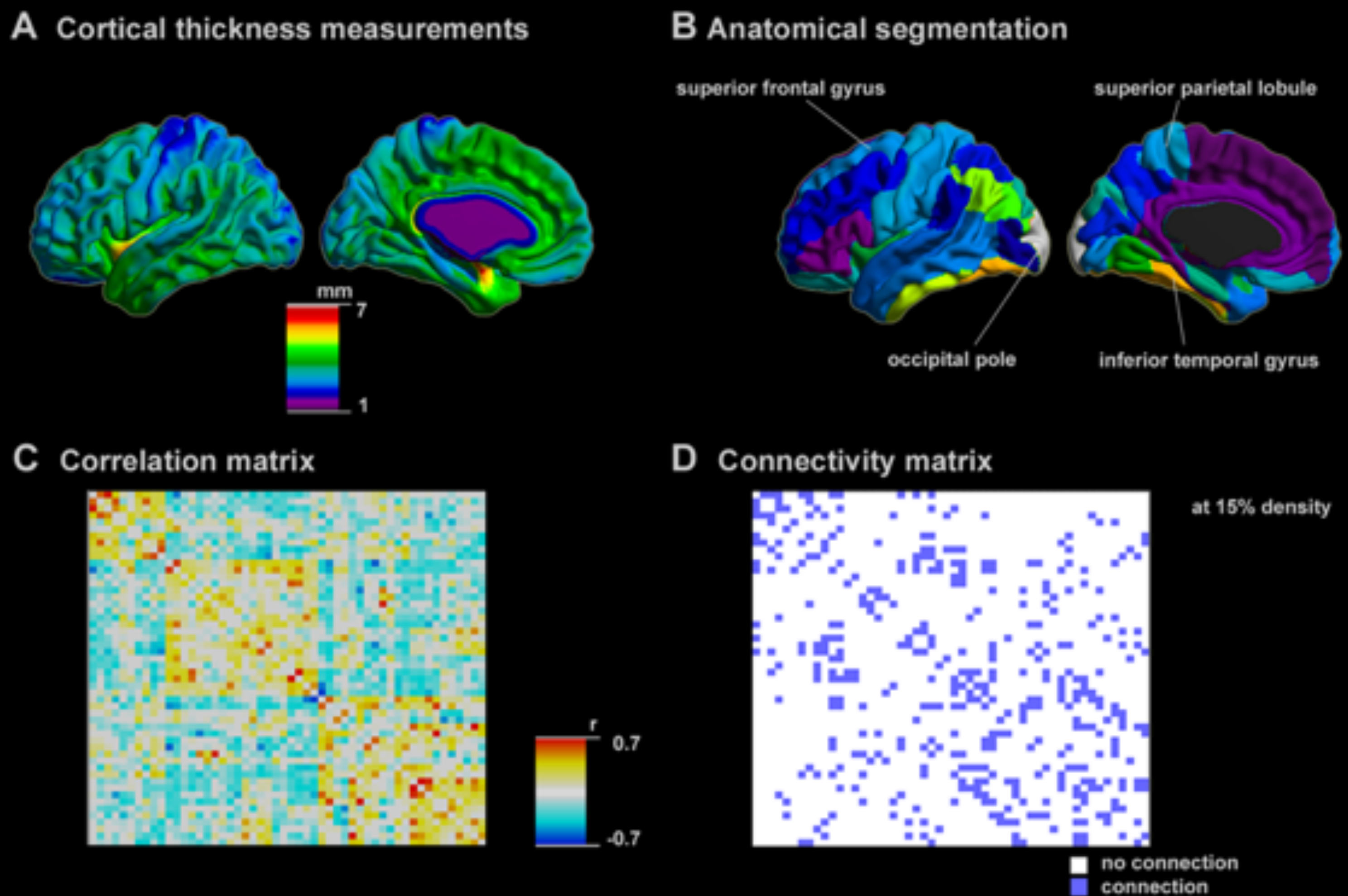
# structural covariance network mapping




Lerch et al. (2006) NeuroImage

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

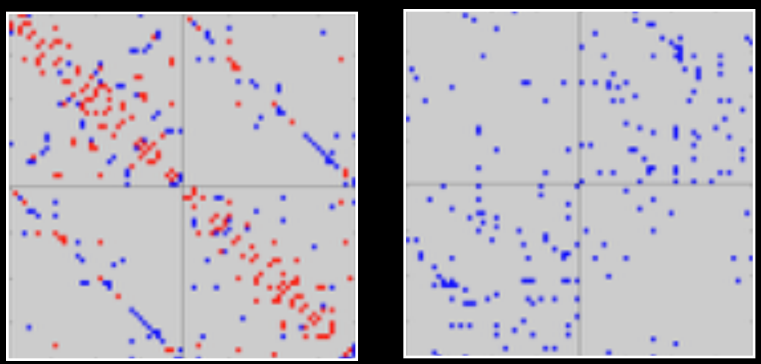
# covariance network construction

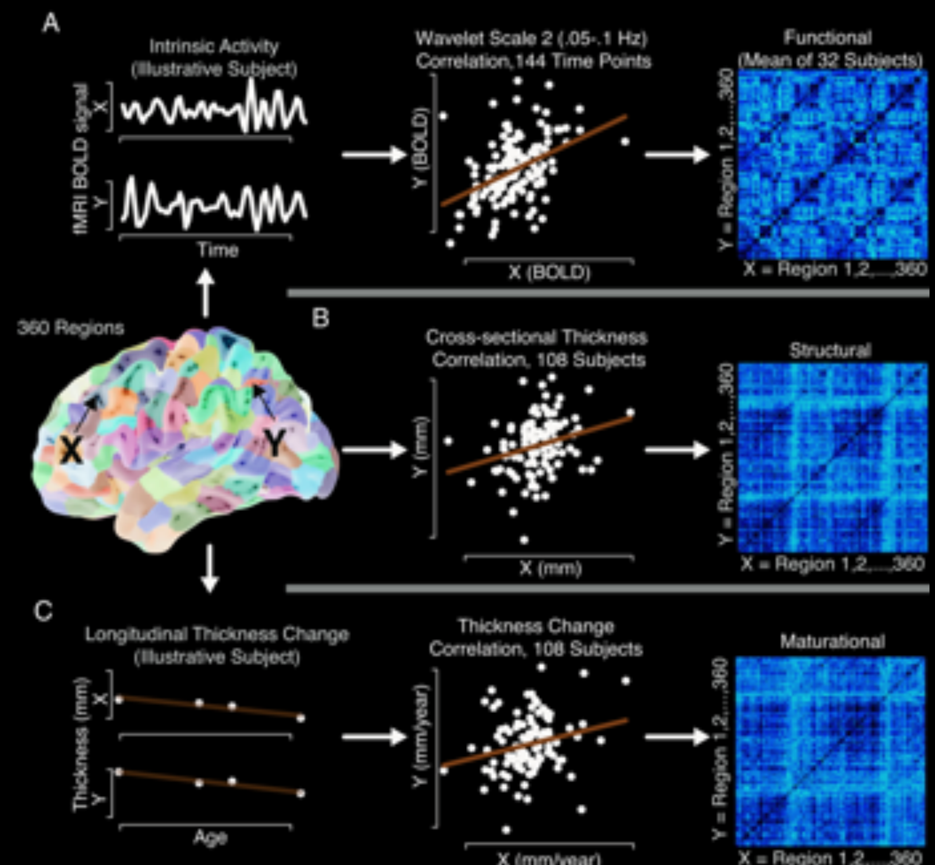


# correspondence to other MRI networks

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 processing and modeling
- seeding from within grey matter regions
- process-based interpretation (e.g., maturation)
- T1w-MRI less artifacts than epi-MRIs

Cons

- no direct correspondence with anatomical connections
- restricted to group-level analysis (but see, Tijms et al. 2011)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# Structural markers of individual differences in self-generated thought

Bernhardt, Smallwood, Tusche, Ruby, Engen, Steinbeis, Singer (2014) NeuroImage

# structural substrates of individual differences

cognitive neuroscience

- most previous studies have assessed functional MRI correlates of cognitive and affective processes
- studies have shown important individual differences in cognition
- biological basis of such differences incompletely understood

structural MRI has been underused in cognitive neuroscience

# everyday thinking

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

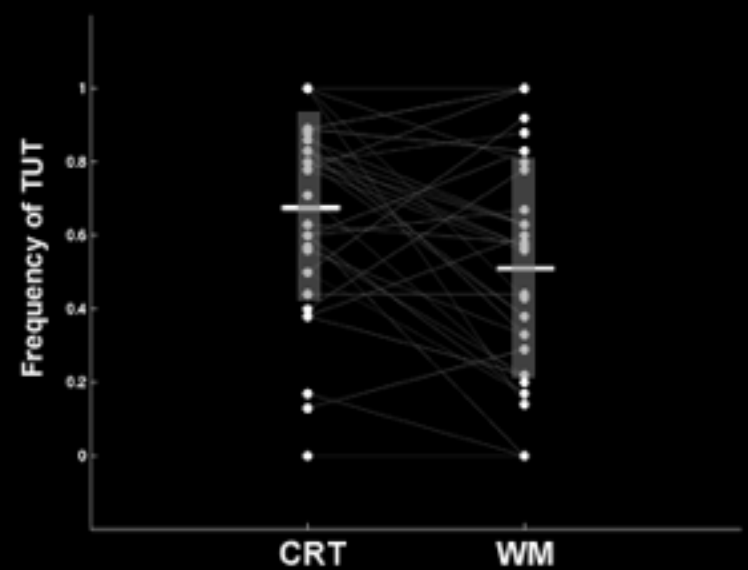
previous work has shown links between mind-wandering and

... creativity, future thinking, and economic decision making

decoupled thought may relate to mPFC activity (Christoff 2009; Schacter 2012)

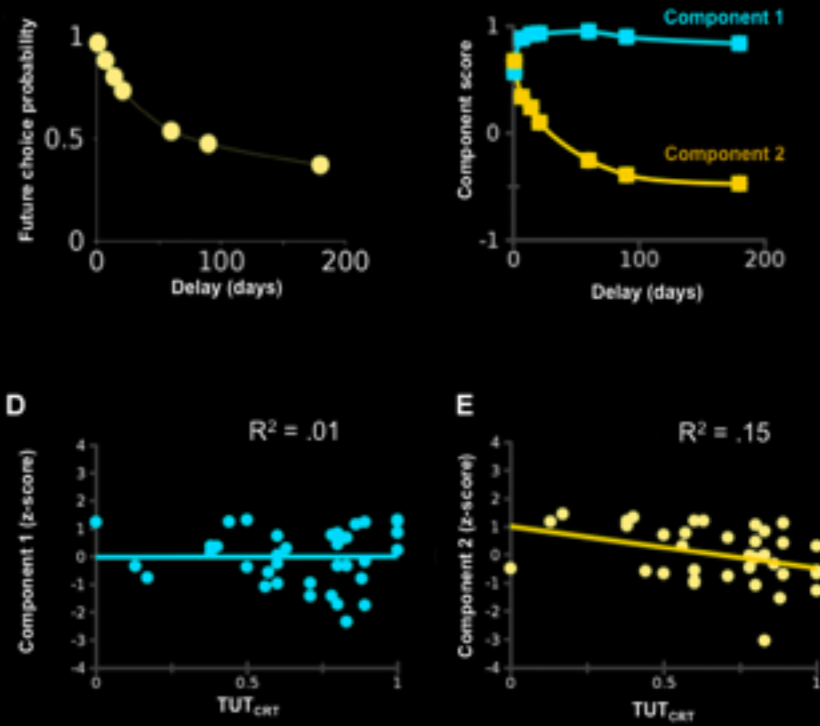
mPFC activity also shown to relate to temporal discounting (Kable and Glimcher 2007)

# mind-wandering



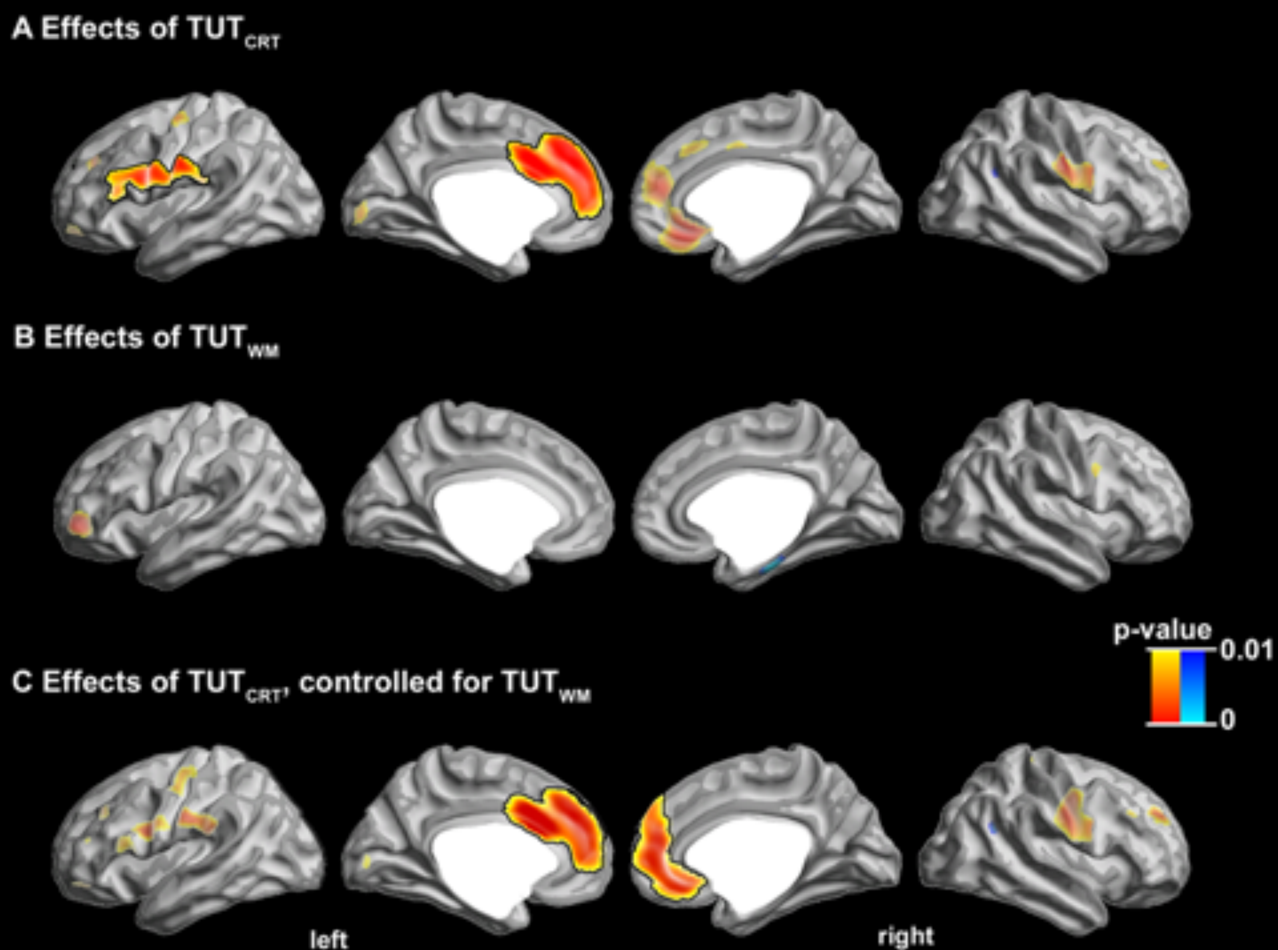

Bernhardt, Smallwood, et al. (2014) NIMG

# ...and patient decision making



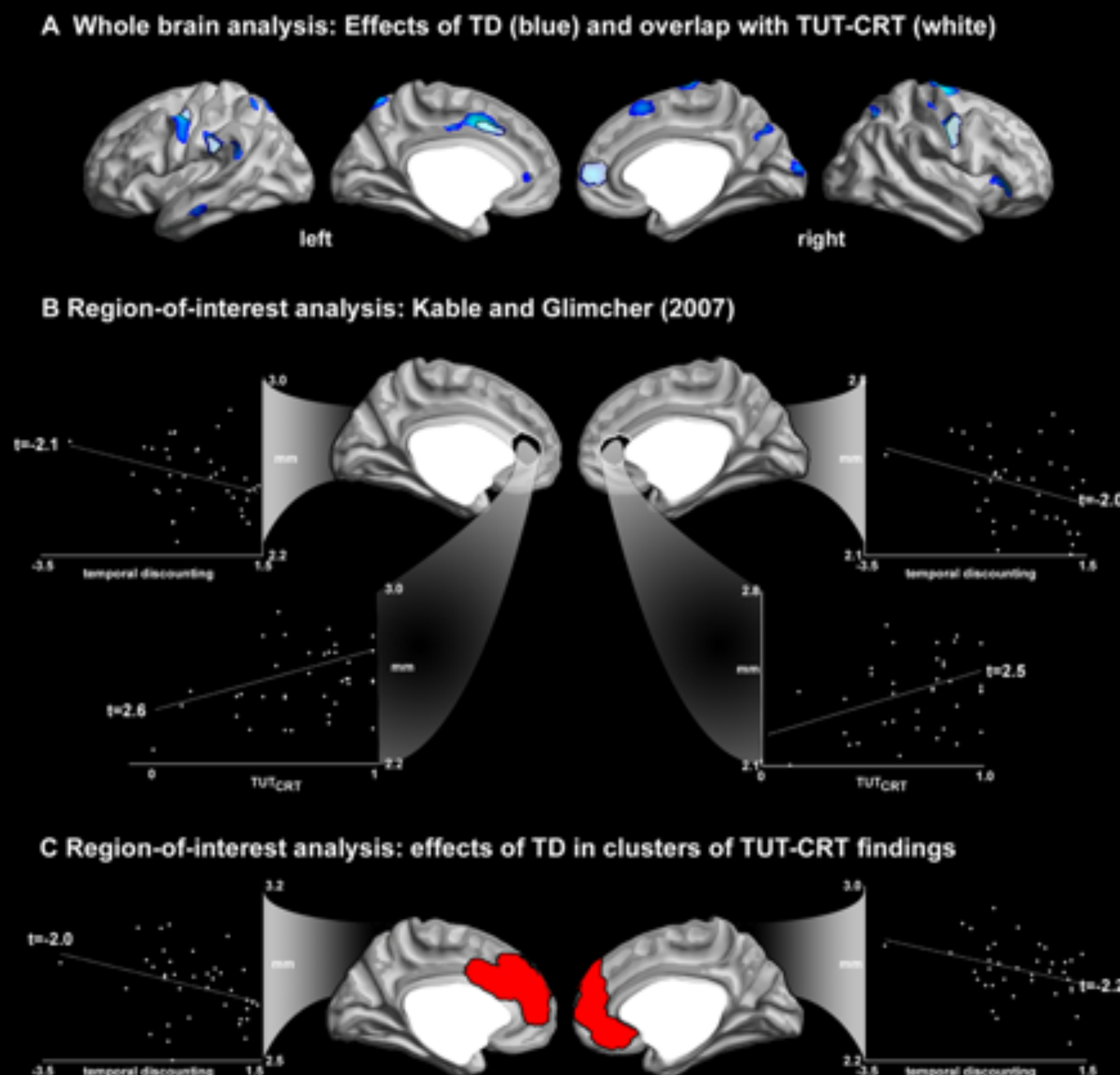

Bernhardt, Smallwood, et al. (2014) NIMG

# substates of TUT




Bernhardt, Smallwood, et al. (2014) NIMG

# overlap with substrates of discounting



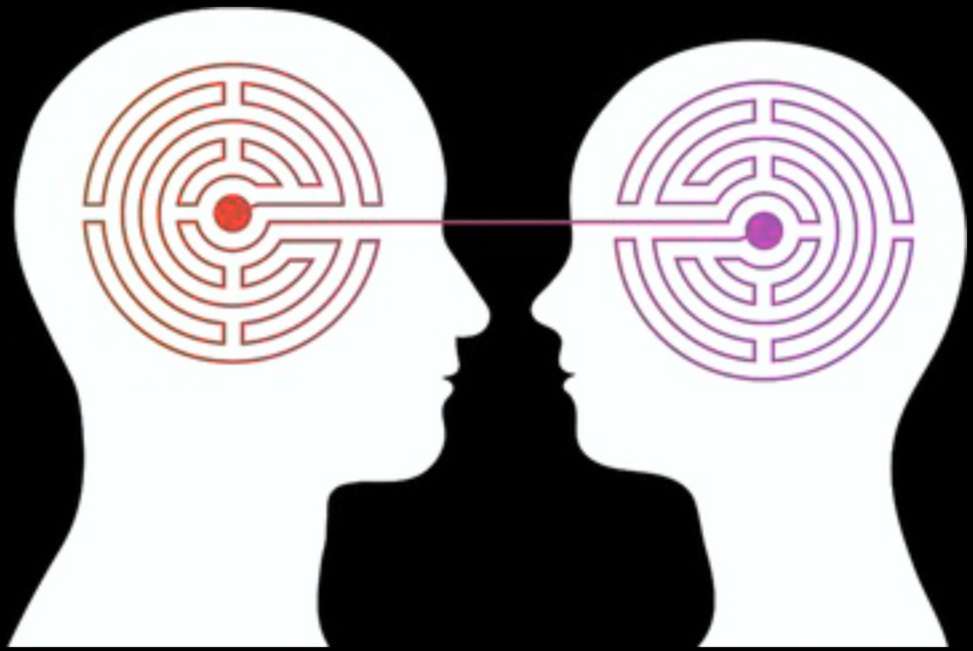
# conclusion

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 mPFC/ACC in decoupled thought
- domain-general control
- important role in evaluation of information from memory



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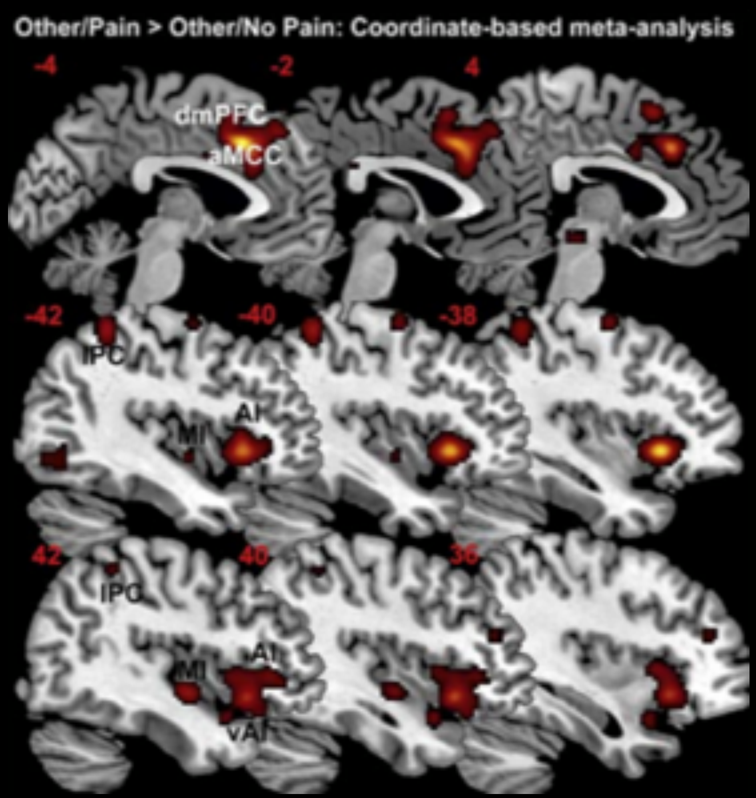
# Structural network markers of individual differences in empathy

Bernhardt, Klimecki, Leiberg, Singer (2013) Cerebral Cortex

# empathy for pain

previous fMRI studies: empathy for pain activates pain matrix

fMRI meta-analyses: most consistent activations in dAI and aMCC




Lamm, Decety, Singer (2011) NIMG

# structural empathy networks

some studies have also shown a relationship between fMRI activations and individual differences in empathy

structural basis of such differences is unclear

given that empathic responding requires integration of multiple processes, analyzing structural networks may be important avenue

Lamm, Decety, Singer (2011) NIMG

# structural empathy networks

94 women, 18-35 years

Empathy

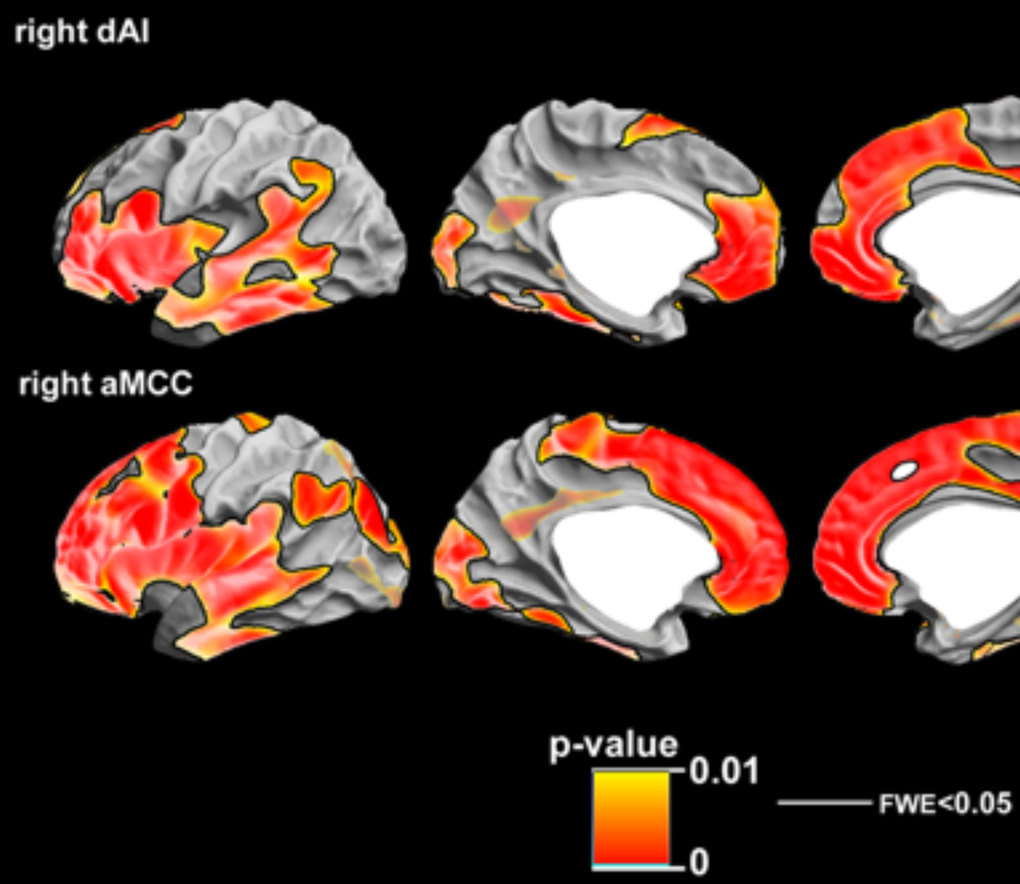
- SoVT task
- Davis' IRI

MRI

- 3Tesla high-resolution T1-weighted MRI available
- structural covariance analysis
- seeds in dAI and aMCC based on Lamm's meta analysis

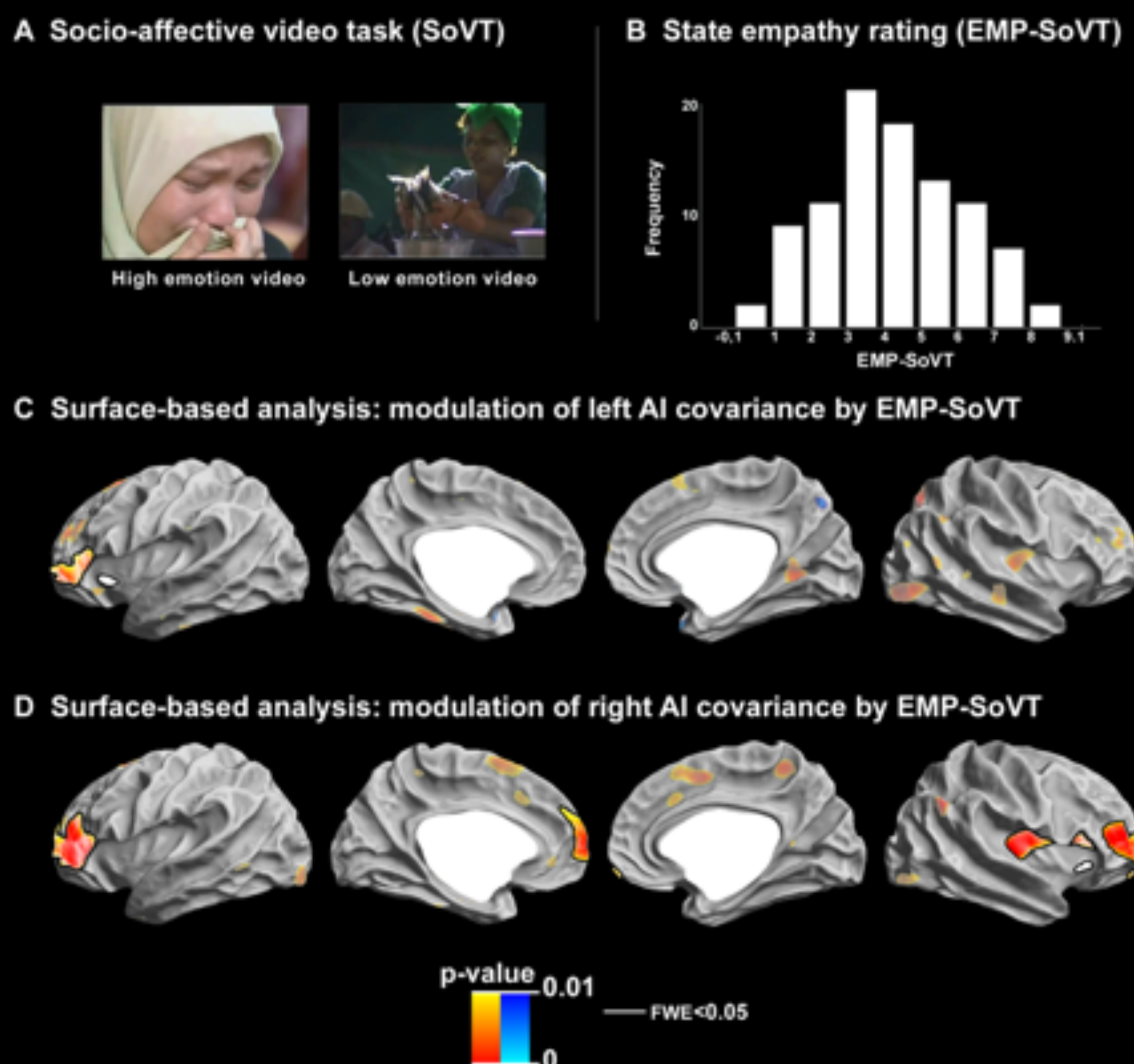
Lamm, Decety, Singer (2011) NIMG

# structural empathy networks



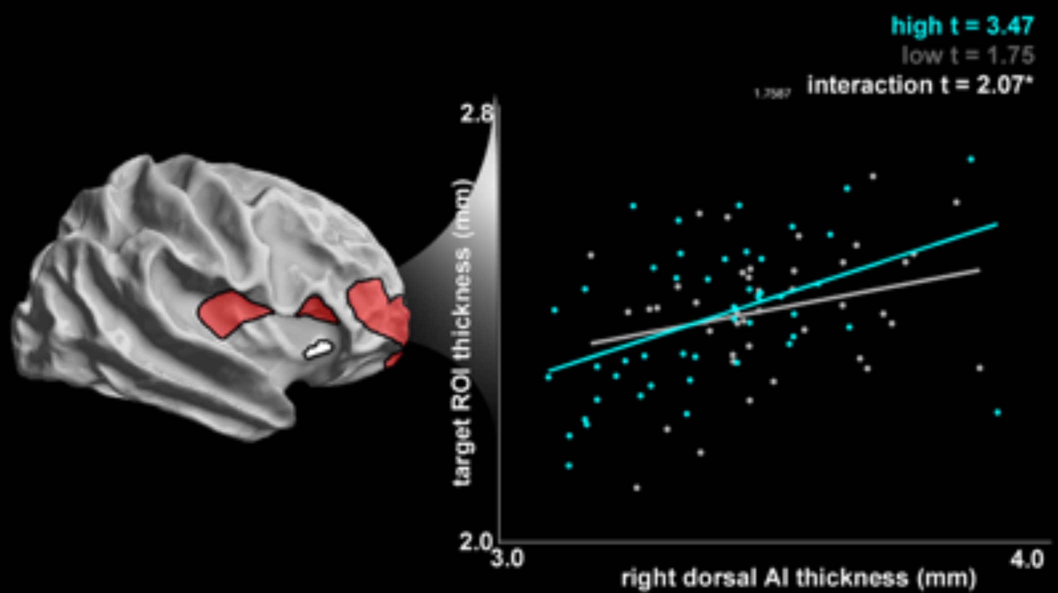

Bernhardt, Klimecki, Leiberg, Singer (2013) Cerebral Cortex

# modulations by state empathy (SoVT)




Bernhardt, Klimecki, Leiberg, Singer (2013) Cerebral Cortex

# modulations by trait empathy (IRI-EC)




Bernhardt, Klimecki, Leiberg, Singer (2013) Cerebral Cortex

# conclusions

covariance networks in dAI and aMCC in large sample of women

dAI covariance scaled by individual differences in state and trait empathy

similar pattern left and right dAI, robust after controlling for whole brain thickness and individual differences in negative affect, similar in state and trait

mostly to medial and lateral PFC as well as posterior insular cortex: possibly more persistent cross-talk between these regions in high empathizers

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Autism Brain Imaging
Data Exchange

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# Structural network alterations in autism spectrum disorders

Valk, diMartino, Singer, Bernhardt (in preparation)

# Background

- ASC prevalent neurodevelopmental disorder
- Core symptoms: impaired social cognition (Frith and Frith 2003)
- Functional MRI studies have consistently shown atypical activations in socio-cognitive networks (Kana 2009, Lombardo 2011)
- Structural substrates less clear
  - $\uparrow$GM (Duerden 2012), $\downarrow$GM (Scheel 2011), no change (Doyle-Thomas 2013)
  - Only limited studies on structural network disruptions
  - Age-related effects unclear
- Studies generally had small sample size and different age ranges

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# Purpose

- Carry out comprehensive mapping of
  - structural differences
  - structural network alterations
  - age-related structural changes in ASD
- Address robustness of findings across different age ranges and centers study by taking advantage of multi-centric open-access data

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# Methods: subjects

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Abide base set

- 16 centers (n=1112; 539 ASC,573 controls, age 6-50 years)
- T1-weighted MRI and resting-state functional MRI
- phenotyping information

Pre-selection

- restrict analysis to 3 centers with children and adults available (n=297)

Final same selection

- take only males and take only acceptable structural MRI (n=220)

# Methods: MRI processing

- FreeSurfer-based cortical thickness measures
- Run → Corrections → Rerun → Corrections → Rerun
- QC: only cases with score above 6/10 made it into final set

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# Mapping thickness changes

- Surface-based group comparison, corrected for age and center
  - Post-hoc analysis in clusters of findings to assess robustness
  - in each center
  - in kids and adults
  - after additional correction for IQ and global mean thickness

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# Cortical thickening in ASC

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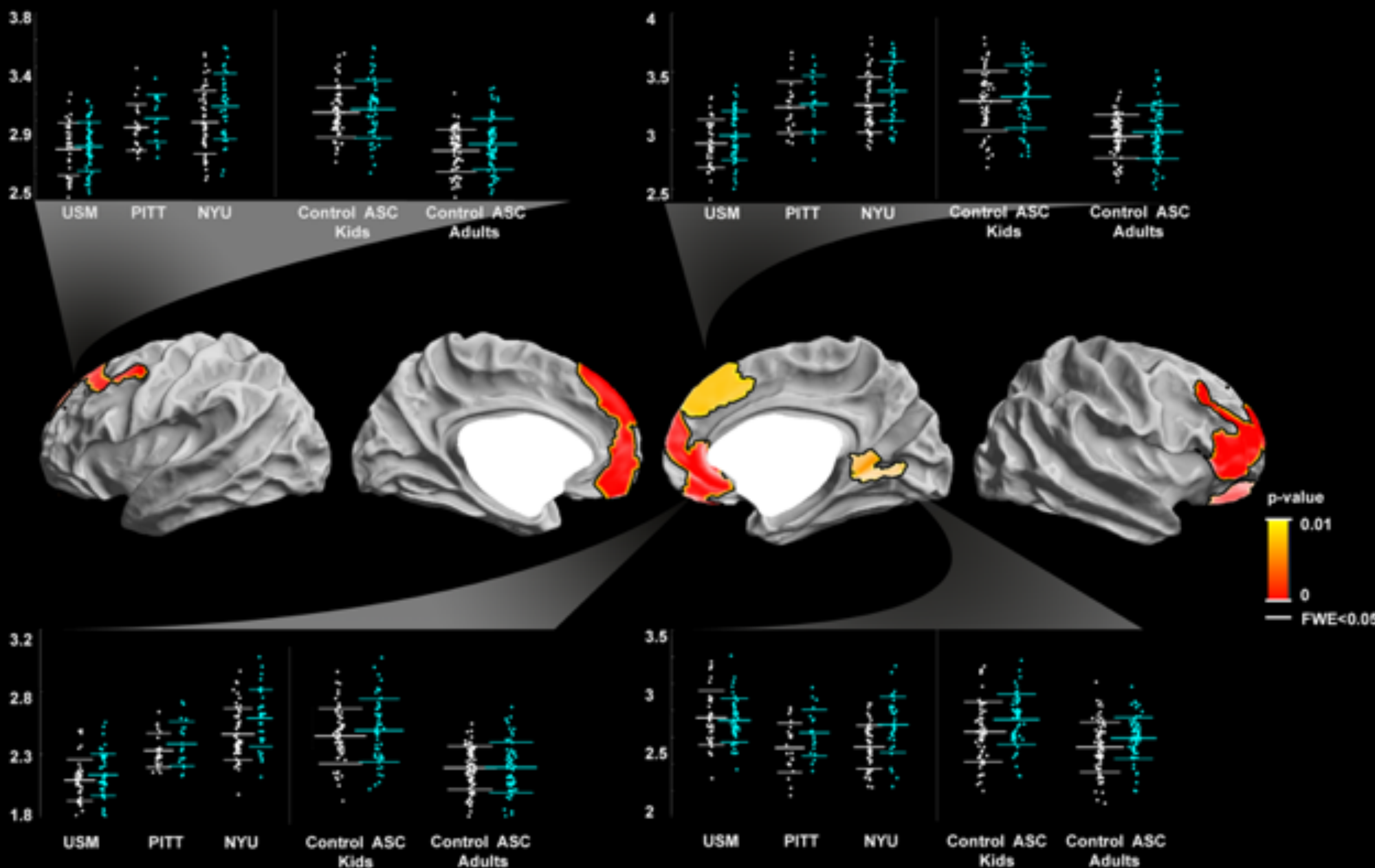

# Covariance network disruptions

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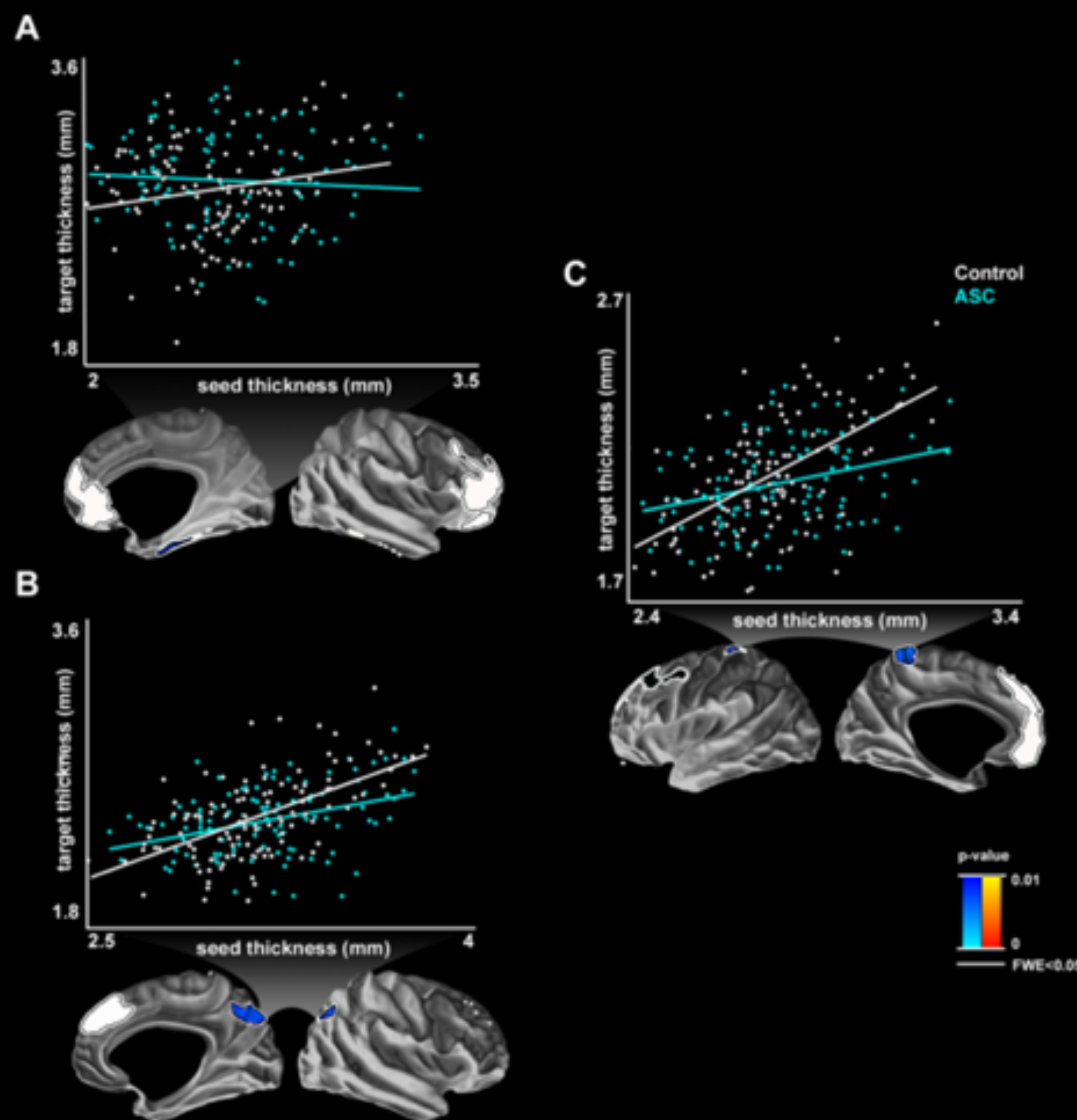

# Summary

- Consistent mPFC cortical thickness increases across all 3 centers and in kids and adults
- mPFC covariance disruptions with inferior temporal, medial parietal, and central regions across all three centers
- no differential effects of ASC diagnosis on age-dependent cortical thickness change

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# Conclusions

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- Multi-centric evidence of local and connectional mPFC disruption
- ↑CT in mPFC: possibly related to early brain overgrowth and incomplete pruning in ASC
- ↓covariance may indicate structural under-connectivity of mPFC with other cortical regions (e.g. PCC/PCU)
- no age-dependent modulation
    - possibly due to large age range studied relative to previous work that has assessed smaller range
- specific and convergent finding of atypical structural network in mPFC in ASC may underly ToM impairment in this condition

overall summary

# overall summary

structural MRI permits

- mapping substrates individual differences
- brain network analysis
- assessing brain pathology
- addressing brain development

- complimentary tools can be used for meaningful analysis
  - MRI volumetry
  - surface-based methods
  - structural MRI covariance analysis

# merci!

Neda and Andrea Bernasconi

Hosung Kim

Seok-Jun Hong

Jessie Kulaga-Yoskovitch

Benoit Caldairou

Min Liu

Luis Concha

Dewi Schrader

Alan Evans

Jason Lerch

Yong He

John Chen

Sebastian Dery

Jeanne Timmins Costello

Fellowship of MNI

Savoy Foundation

Tania Singer

Jonathan Smallwood

Sofie Valk

Nikolaus Steinbeis

Daniel Margulies

Giorgia Silani

Geoffrey Bird

Uta Frith