

Connectomics in Medicine: Pathways, Networks and Beyond

Ragini Verma

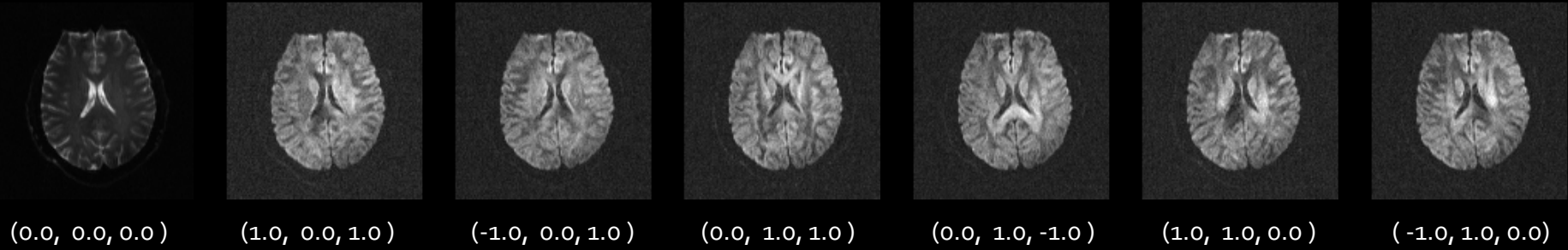
Center for Biomedical Image
Computing and Analytics
Radiology
University of Pennsylvania

Traffic in the Brain

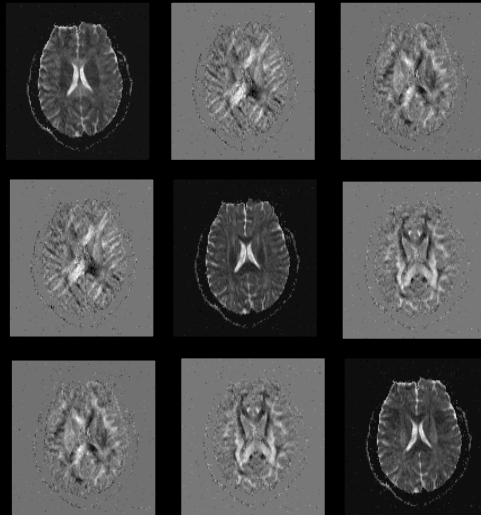


DTI: Diffusion Tensor Imaging

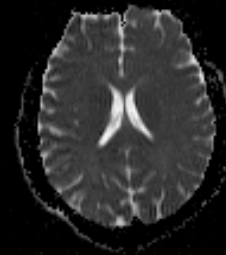
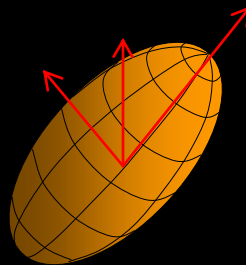
Bo (image without diffusion weighting) and at least 6 gradient directions/slice



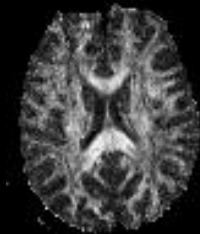
Reconstruct tensor
using the Stejskal-
Tanner equation



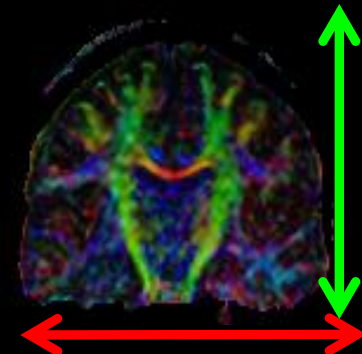
$$D = \begin{bmatrix} d_{xx} & d_{xy} & d_{xz} \\ d_{xy} & d_{yy} & d_{yz} \\ d_{xz} & d_{yz} & d_{zz} \end{bmatrix}$$



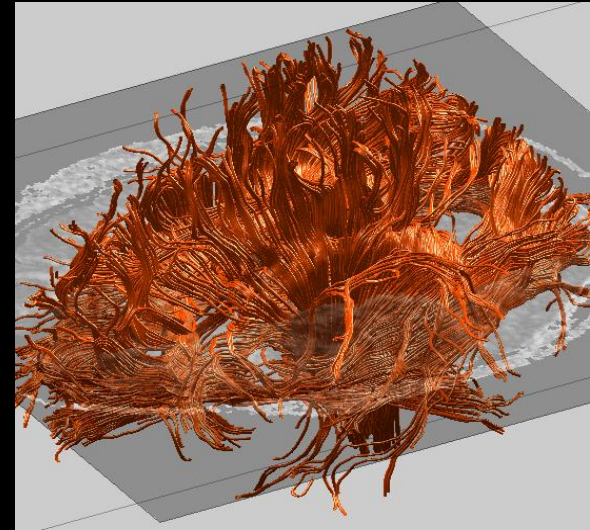
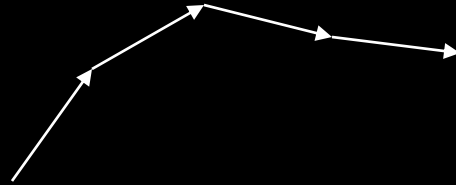
Mean Diffusivity



Fractional Anisotropy



Streamline Tractography

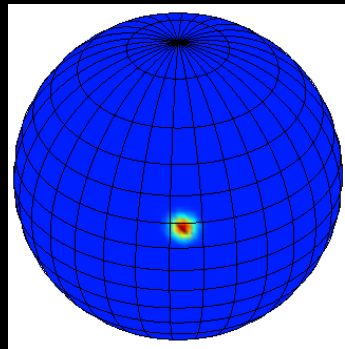
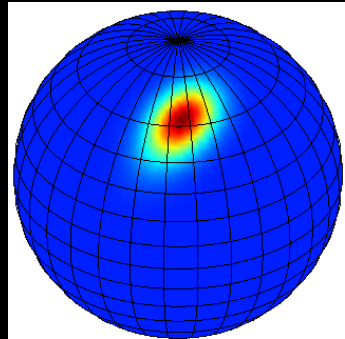
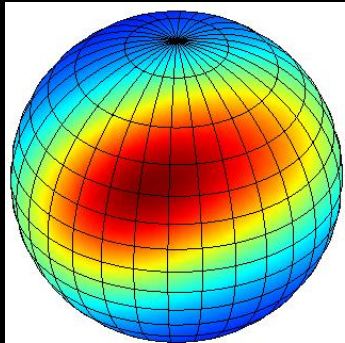


Joining the principal diffusion direction

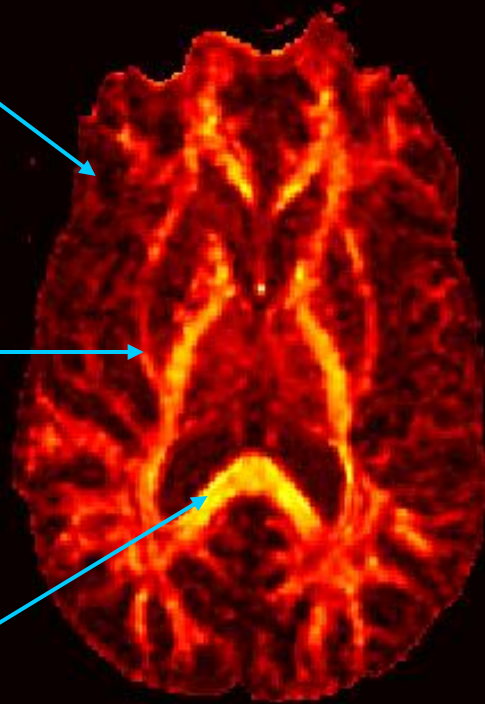
Starting criterion: Region of Interest

Stopping criteria: ROI, curvature of fiber, diffusion measure of anisotropy

Probabilistic tractography

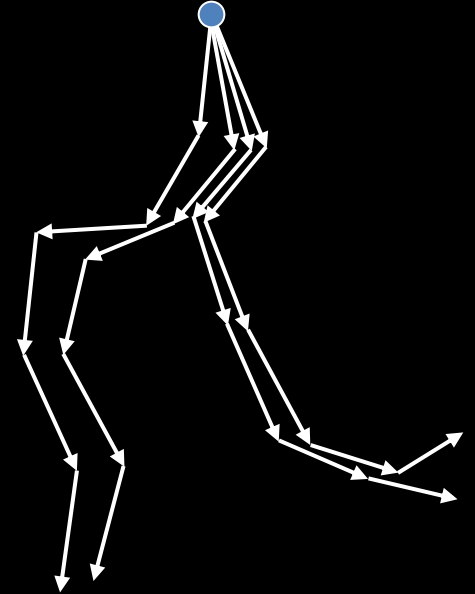


Fractional anisotropy

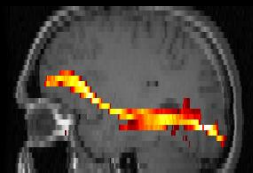


A probability density function of the fiber orientation in each point.

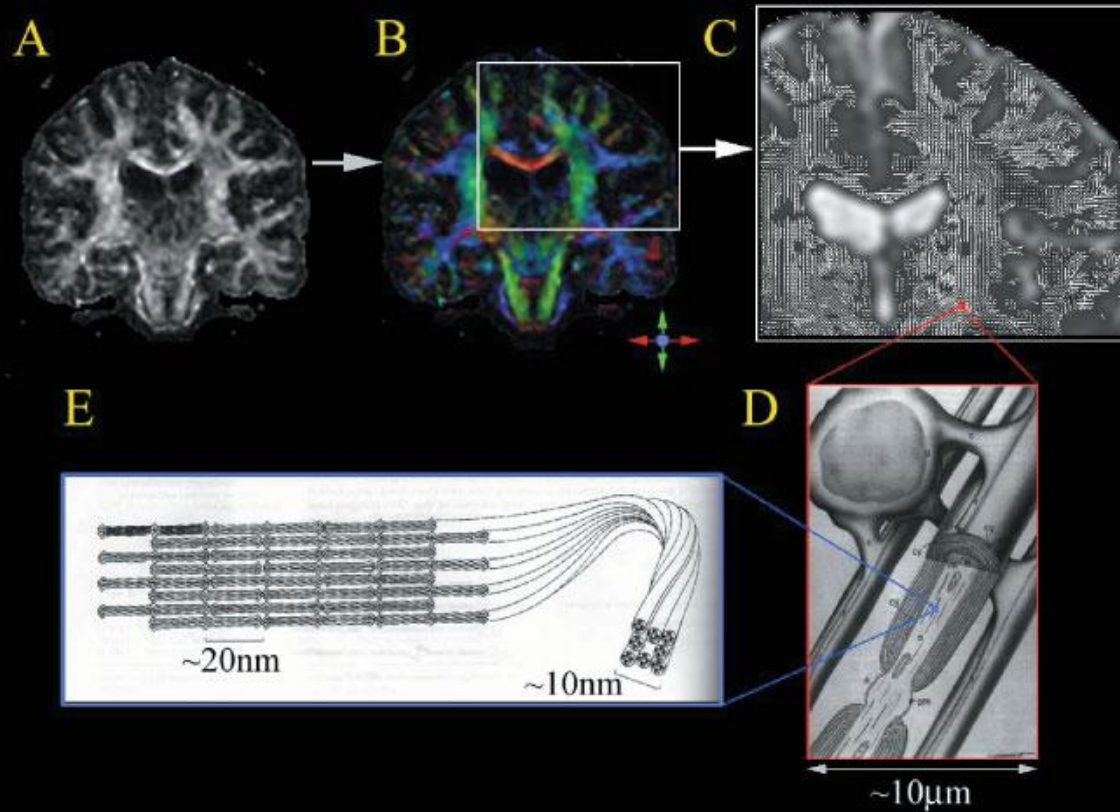
Start point



At every step, draw a step direction from the pdf of the underlying fiber orientation.

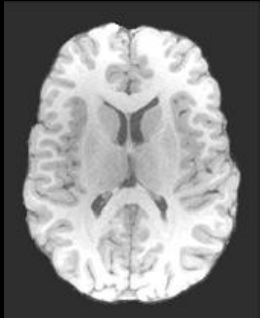


Putting Things in Perspective

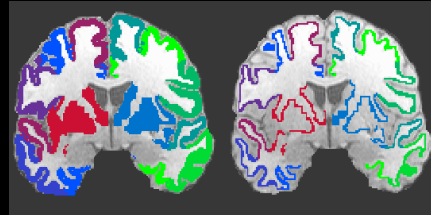
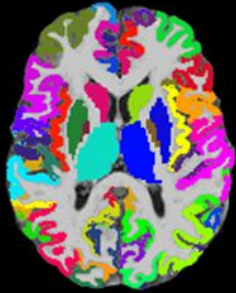


Courtesy Susumu Mori

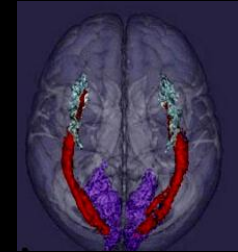
The Structural Connectome



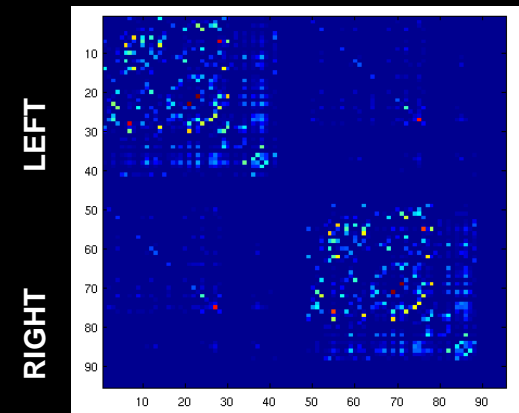
1: Parcellation of T1 structural scan into 95 cortical and sub-cortical regions



2: Transfer of region labels to diffusion space and computing the GM-WM boundary.



3: Probabilistic fiber tracking from each seed ROI i to target ROI j .



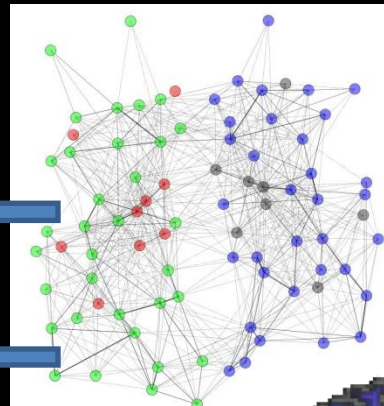
4: Connectivity quantification between each ROI pair (i,j) computed from $P_{ij} * \text{active surface area of the seed}$.

6: Statistics on networks (binarized/weighted)

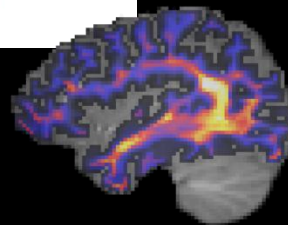
Edge-wise t-test

Topological measures/
Lobe/node-specific
measures

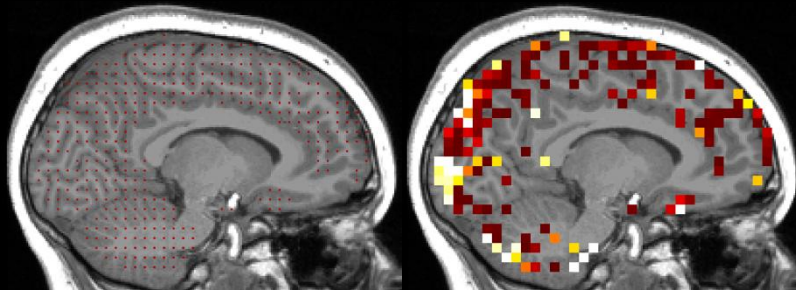
Clustering / pattern
classification



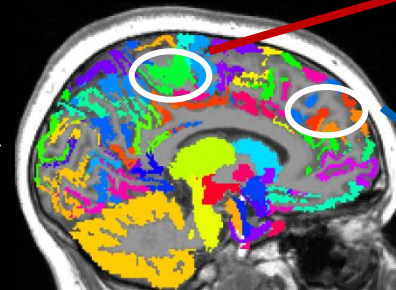
5: Construction of weighted structural connectivity network W



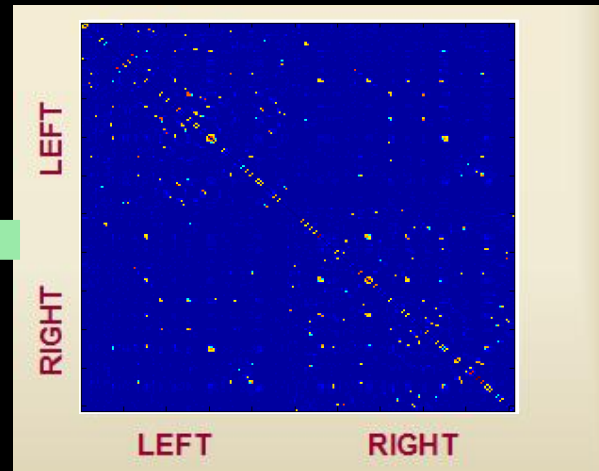
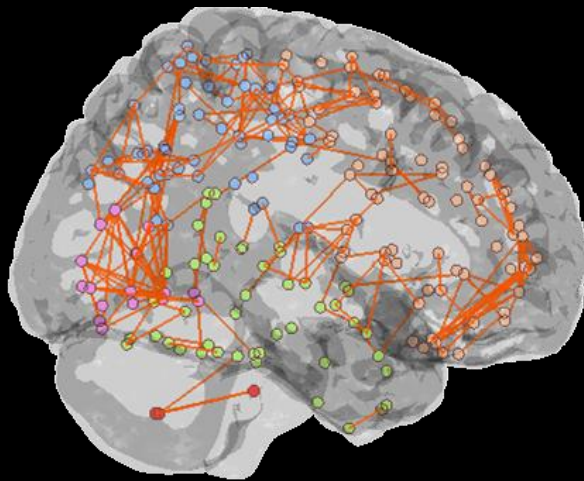
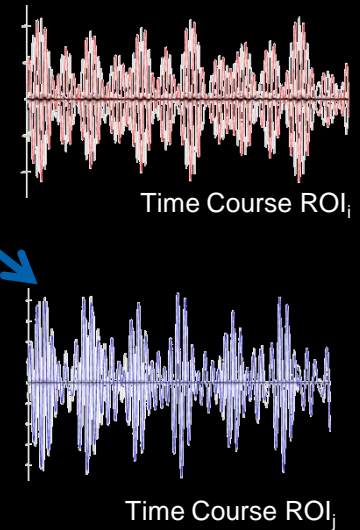
The Functional connectome



1) Localize frequency specific activity and use spatial sparsity pattern to compute inverse operator.

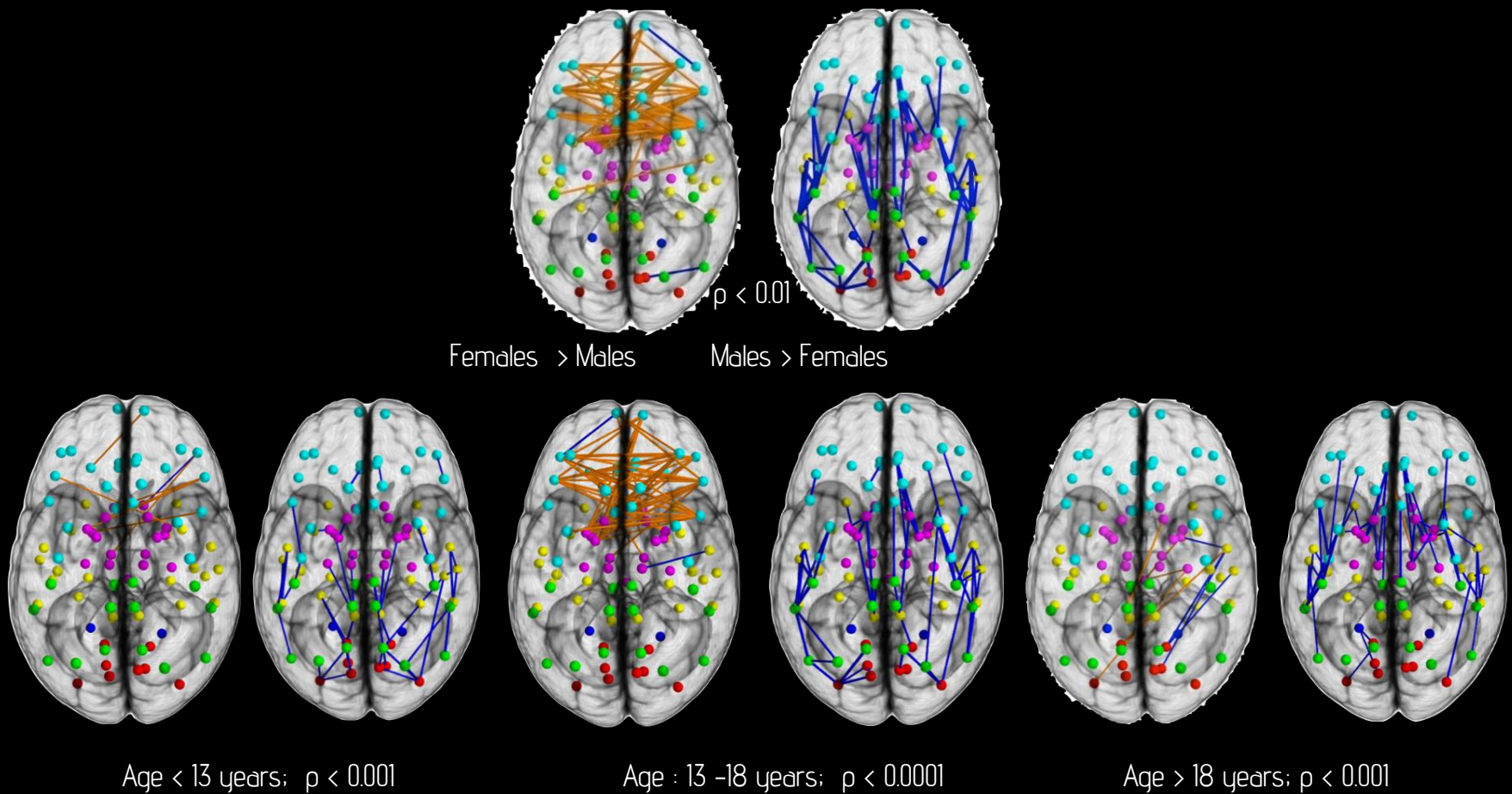


2) Use SVD to extract principal time course for each atlas defined region.



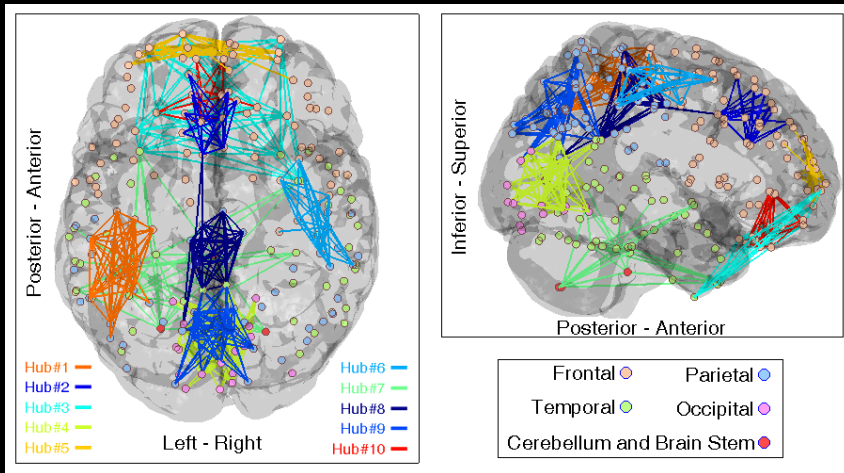
3) Connectivity quantification between each ROI pair (i,j) using Synchronization Likelihood.

Connectome Based Morphometry



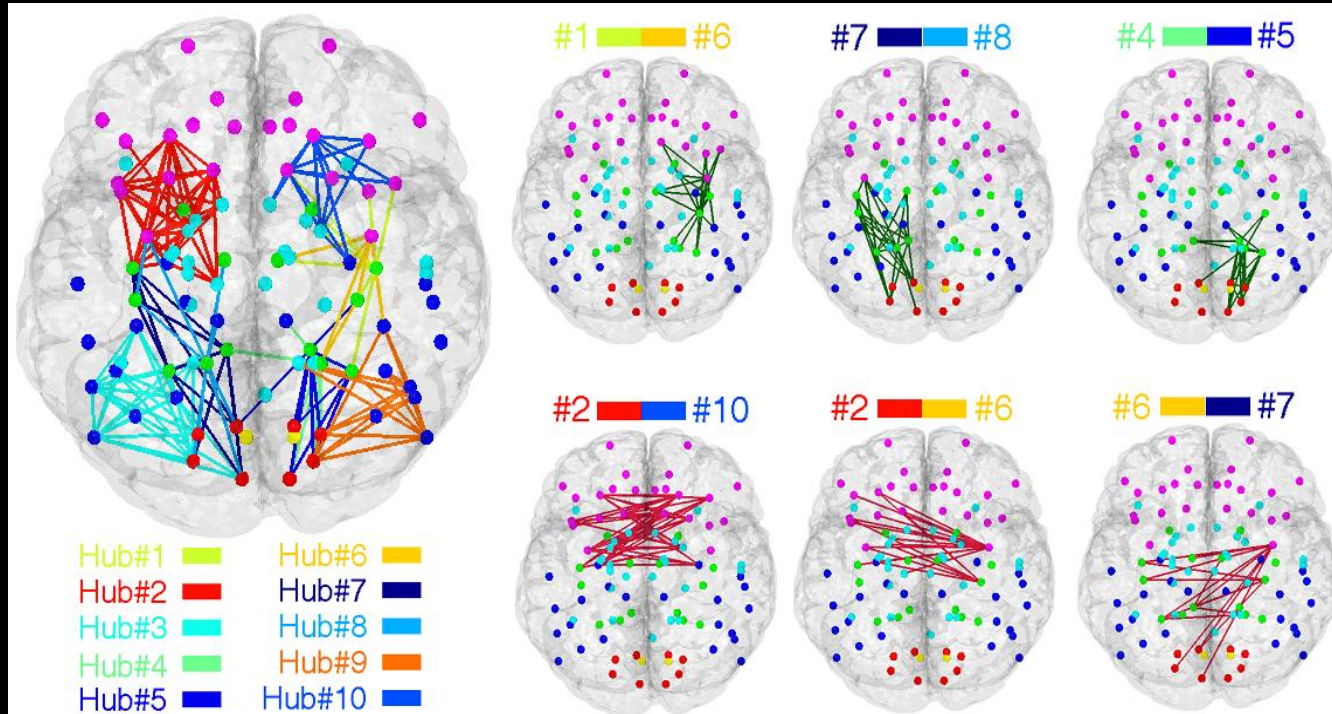
Data: Raquel & Ruben Gur, Neuropsychiatry

Gender Sub-networks

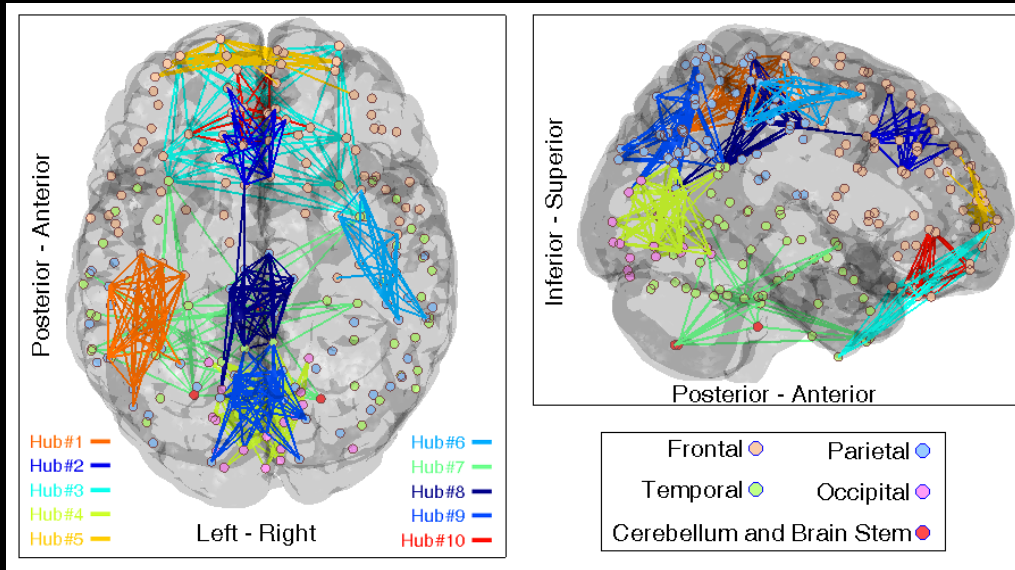


MEG-based
connectivity in
population with
ASD

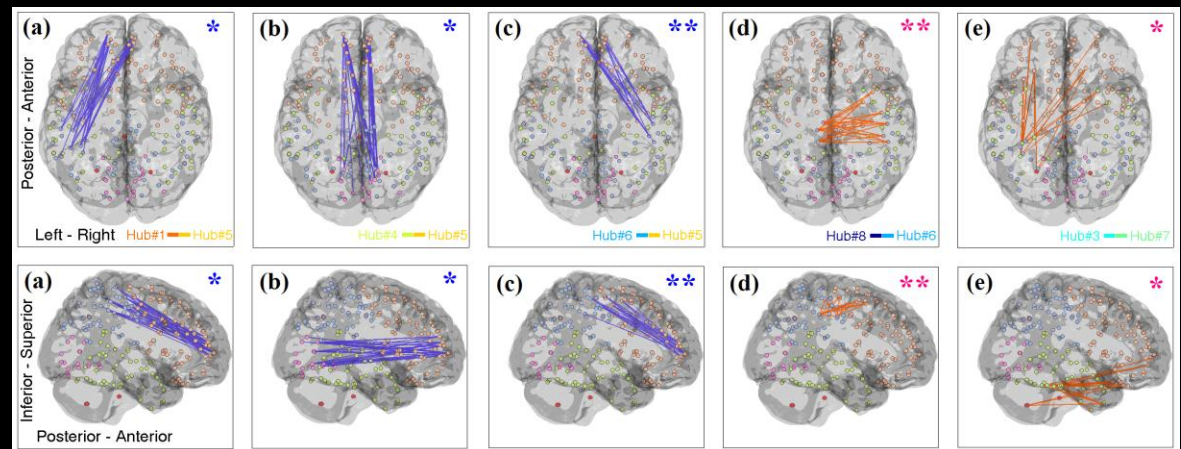
DTI-based
connectivity in a
healthy
population 8-23
years of age



Sub-Networks in Autism

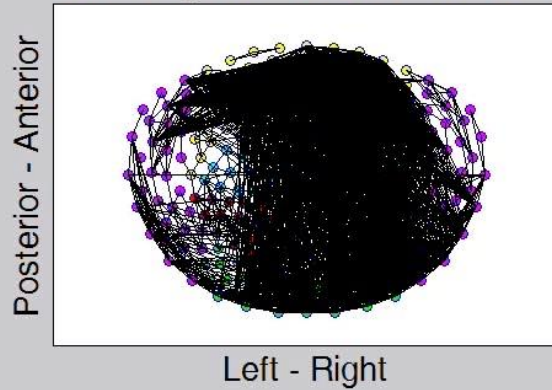


37 ASD
40 TDC
male children aged 6-14 years
(age difference $p > 0.6$)

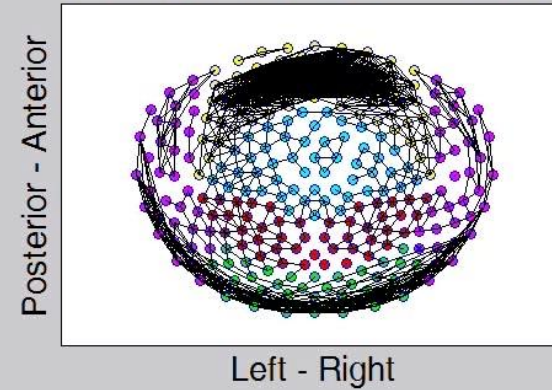


Temporal Dynamics

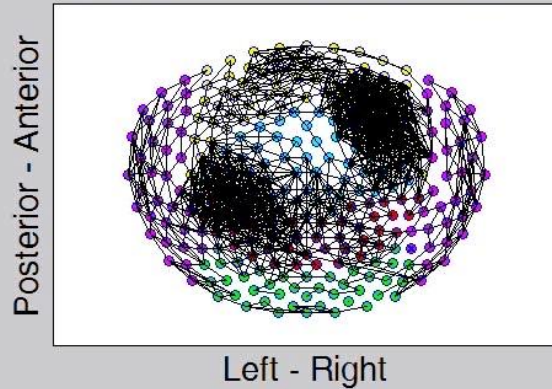
ASD Subject 1 - time instance # 1



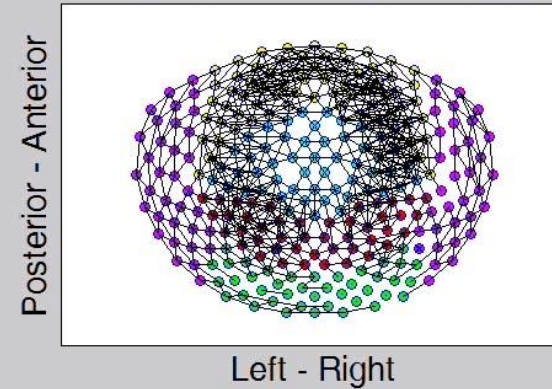
ASD Subject 1 - fulltime - δ band



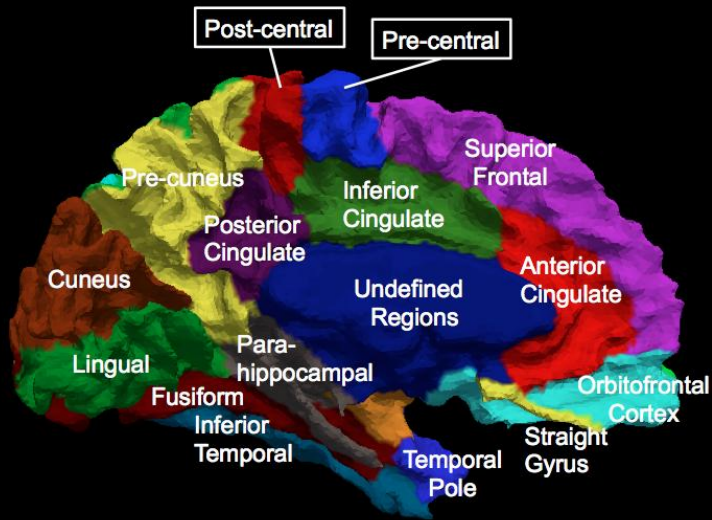
TD Subject 1 - time instance # 1



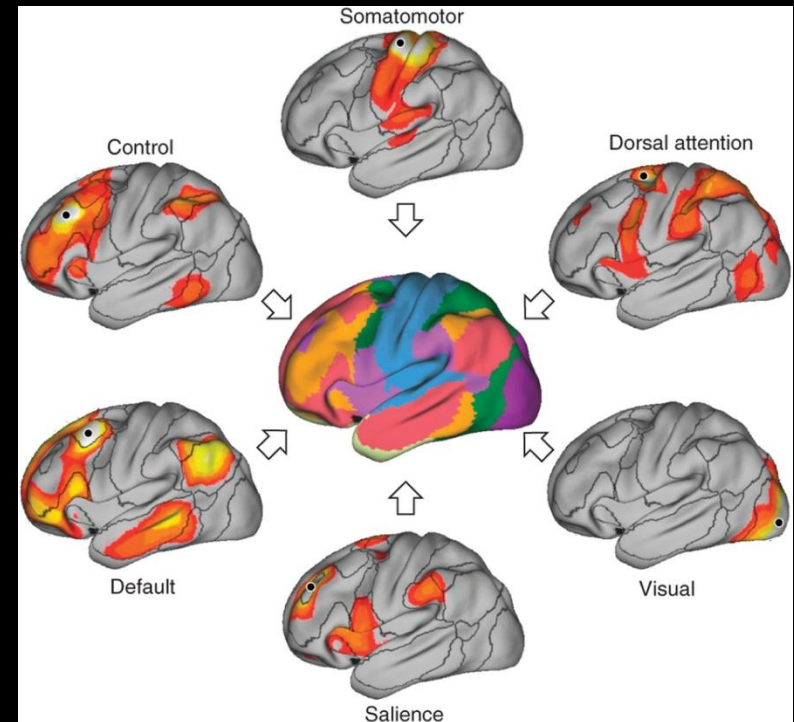
TD Subject 1 - fulltime - δ band



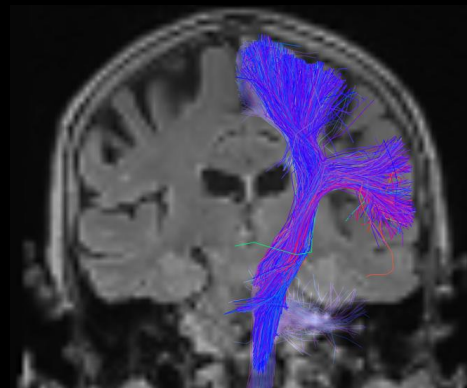
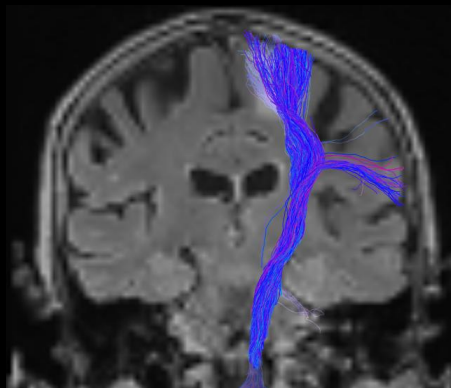
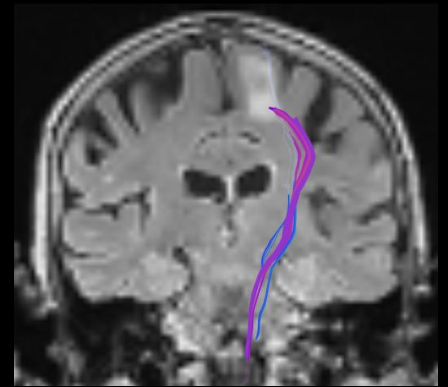
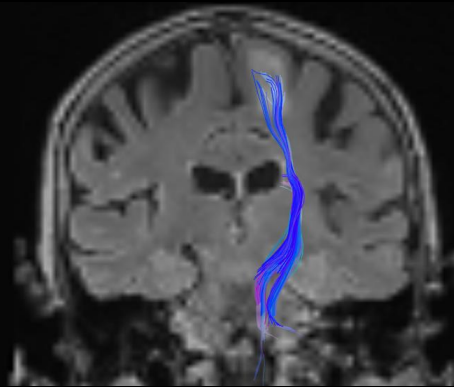
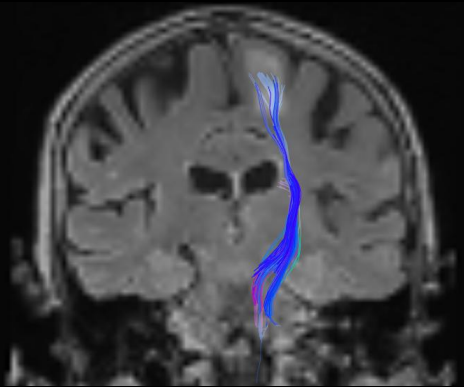
What parcellation to use?



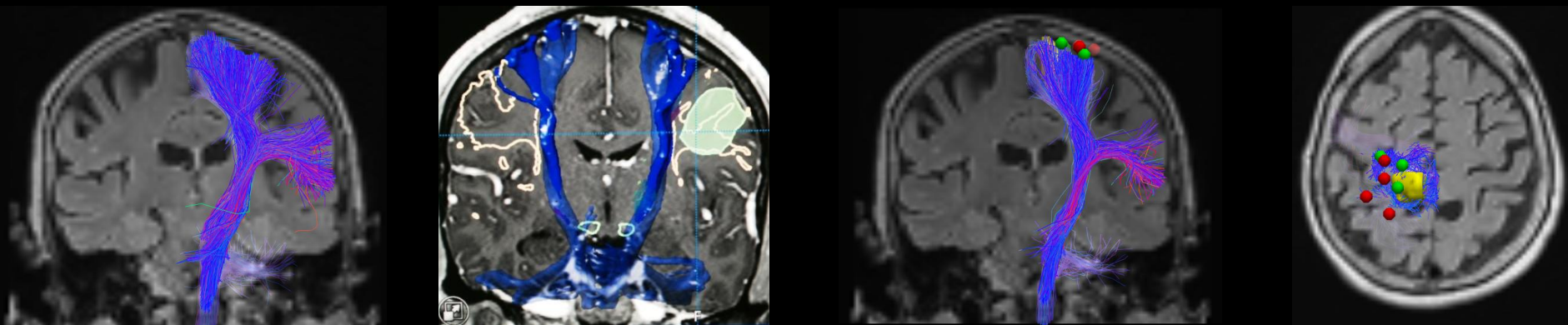
- Resolution of parcellation
- Functional / structural connectivity should be the basis
- Validation?



Finding the “one”

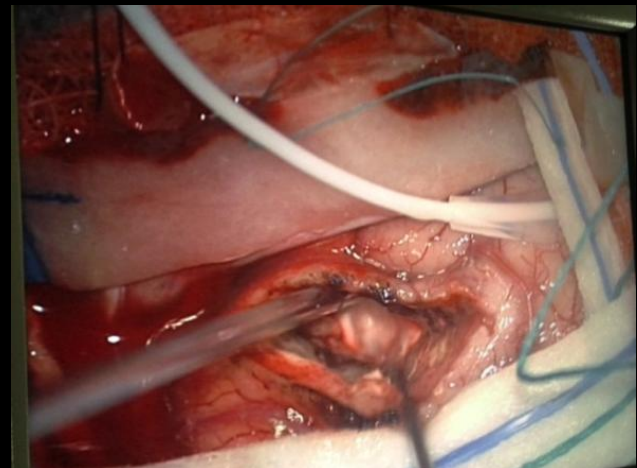
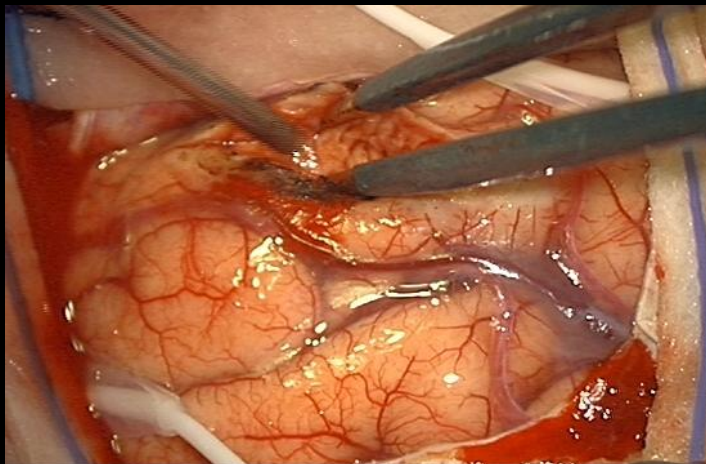
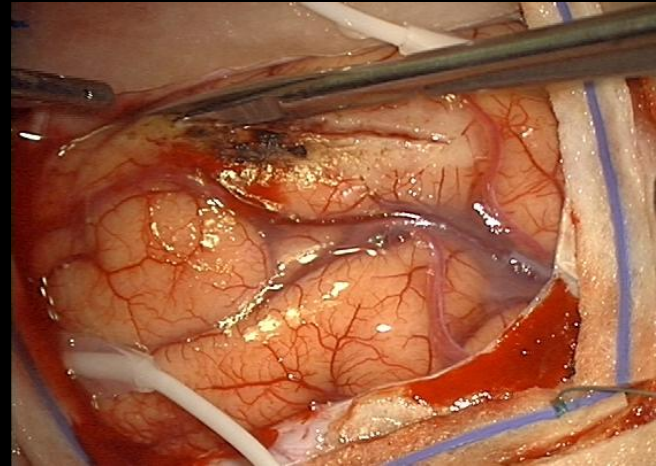
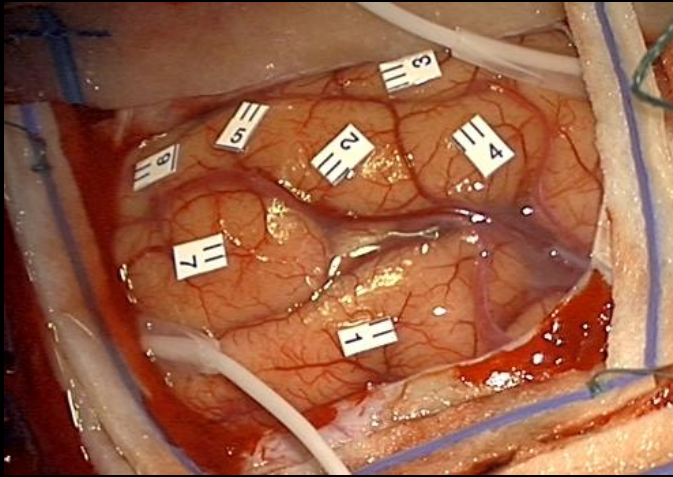


How do we know this is the “one”?

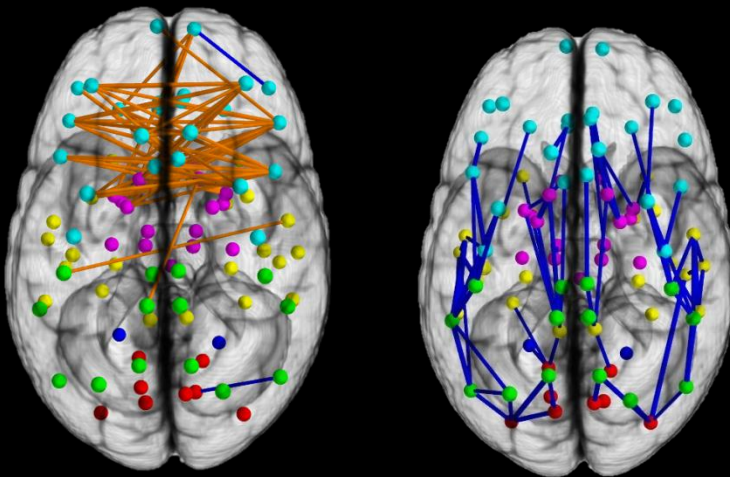


- Validating in humans – not animal models
- What should be the measure of connection strength
- How to validate the connectivity matrix

Putting things back in perspective



What is best method for analysis?



- High dimensionality - multiple comparison correction
- Small sample size
- Posthoc interpretation of graph theory numbers
- Subject-wise variability is not quantified
- Results not always interpretable

So what do we do?

Hypothesis : Ask the question

Validation : Question the answer

Get the neuroscientist and clinician involved!