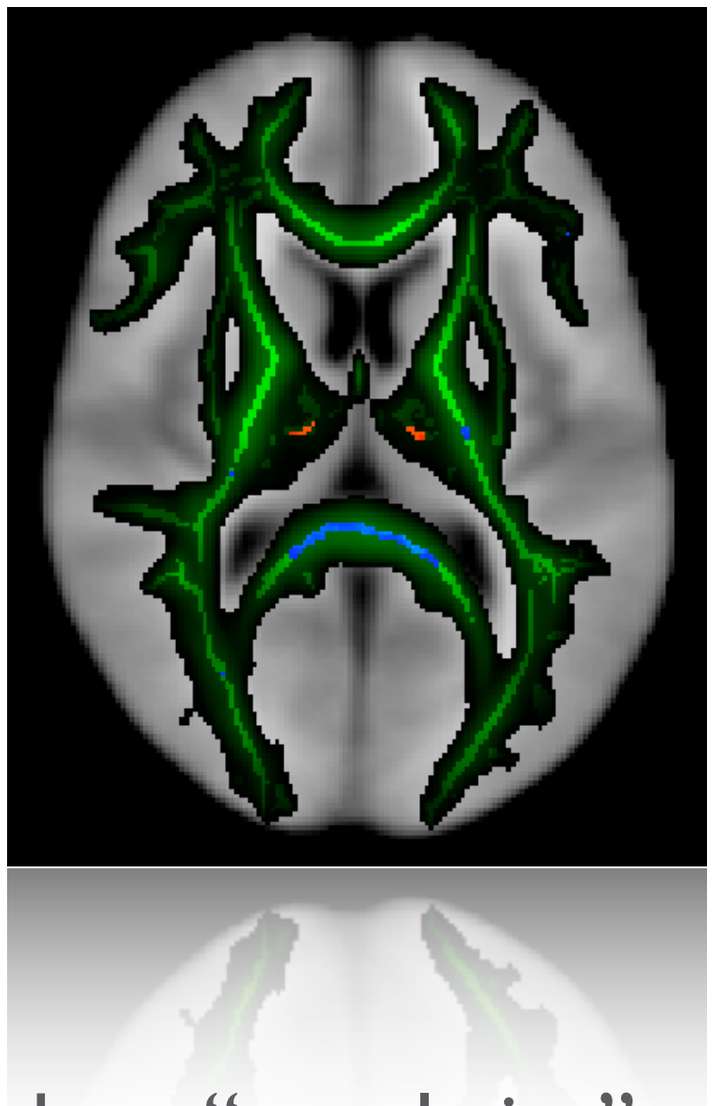
TBSS : Tract-Based Spatial Statisics



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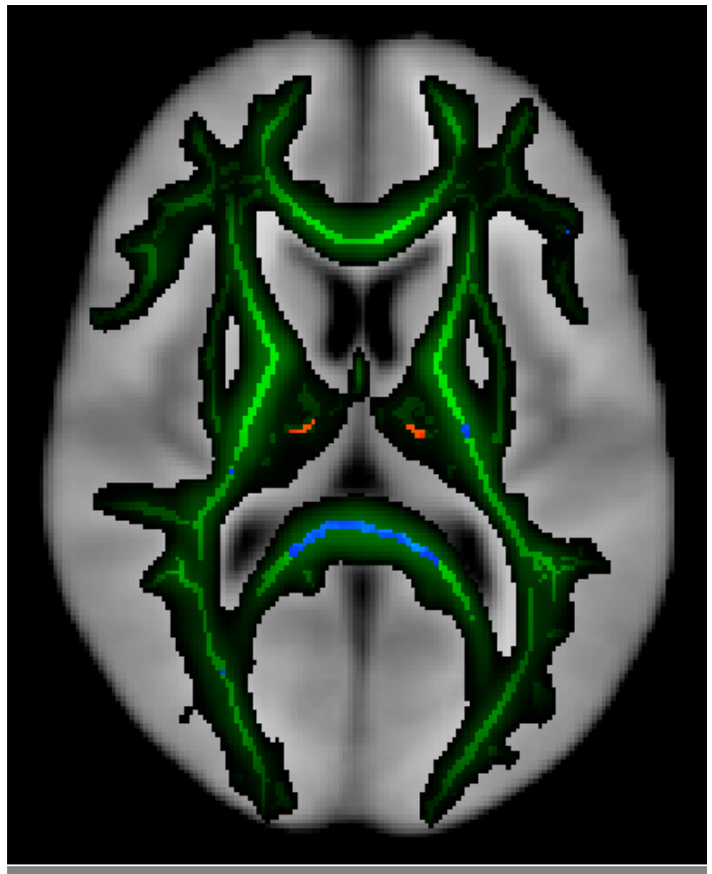

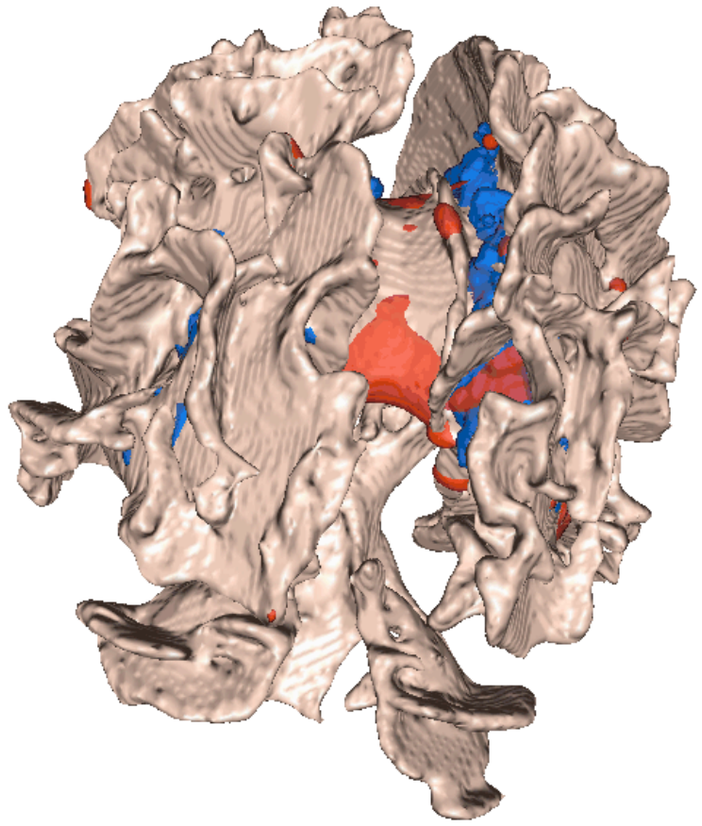

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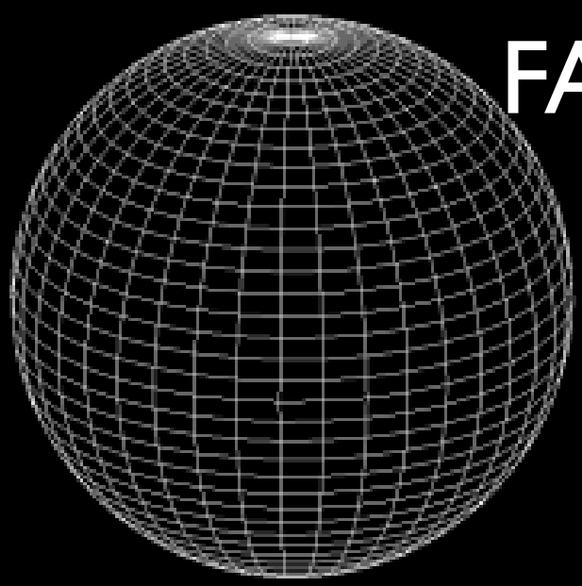
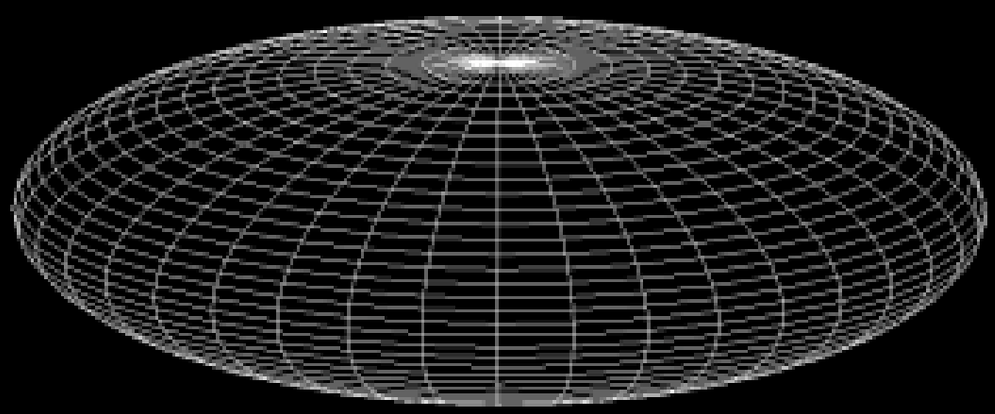
Tensor-derived parameters: Fractional Anisotropy

- FA encodes how strongly directional diffusion is
  - (derived from diffusion tensor eigenvalues)
- Hence good marker for WM integrity
  - i.e., good marker for disease, development, etc.

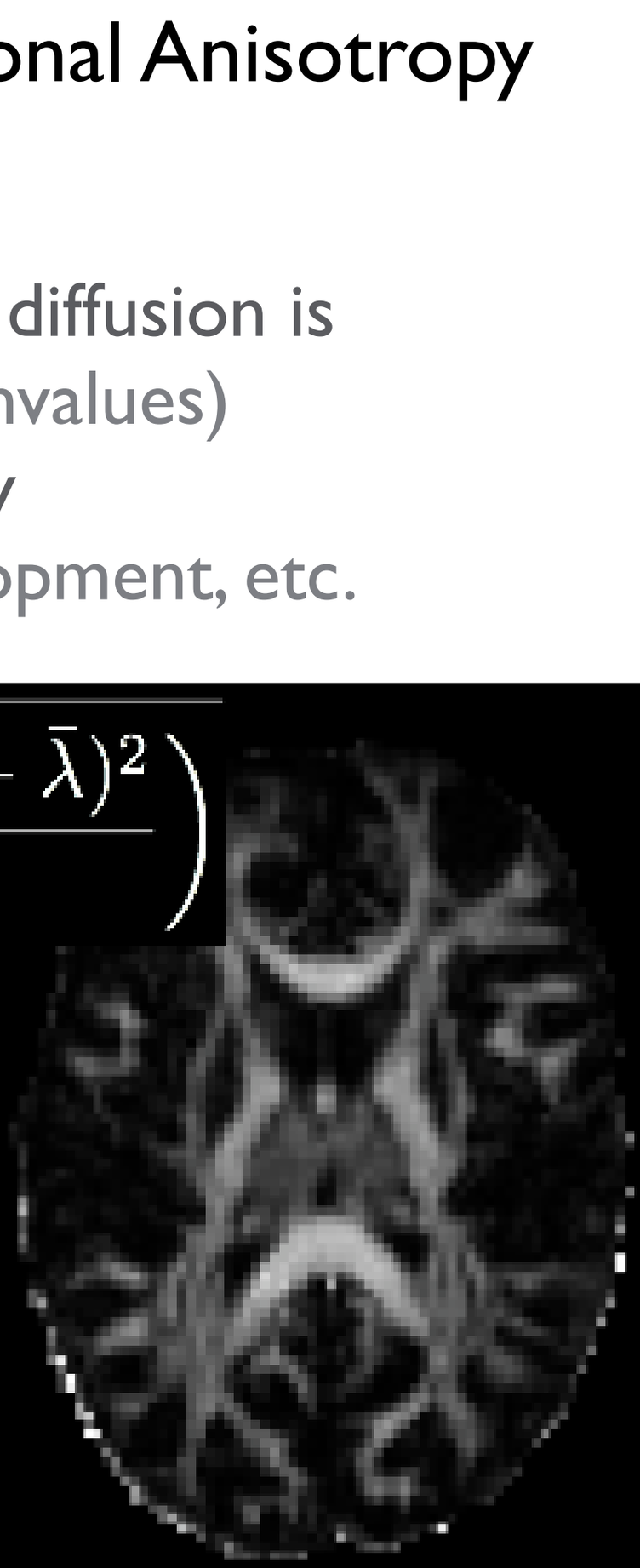
$$\mathrm{FA} = \sqrt{\frac{3}{2}\left(\frac{(\lambda_1-\bar{\lambda})^2+(\lambda_2-\bar{\lambda})^2+(\lambda_3-\bar{\lambda})^2}{\lambda_1^2+\lambda_2^2+\lambda_3^2}\right)}$$



FA=0

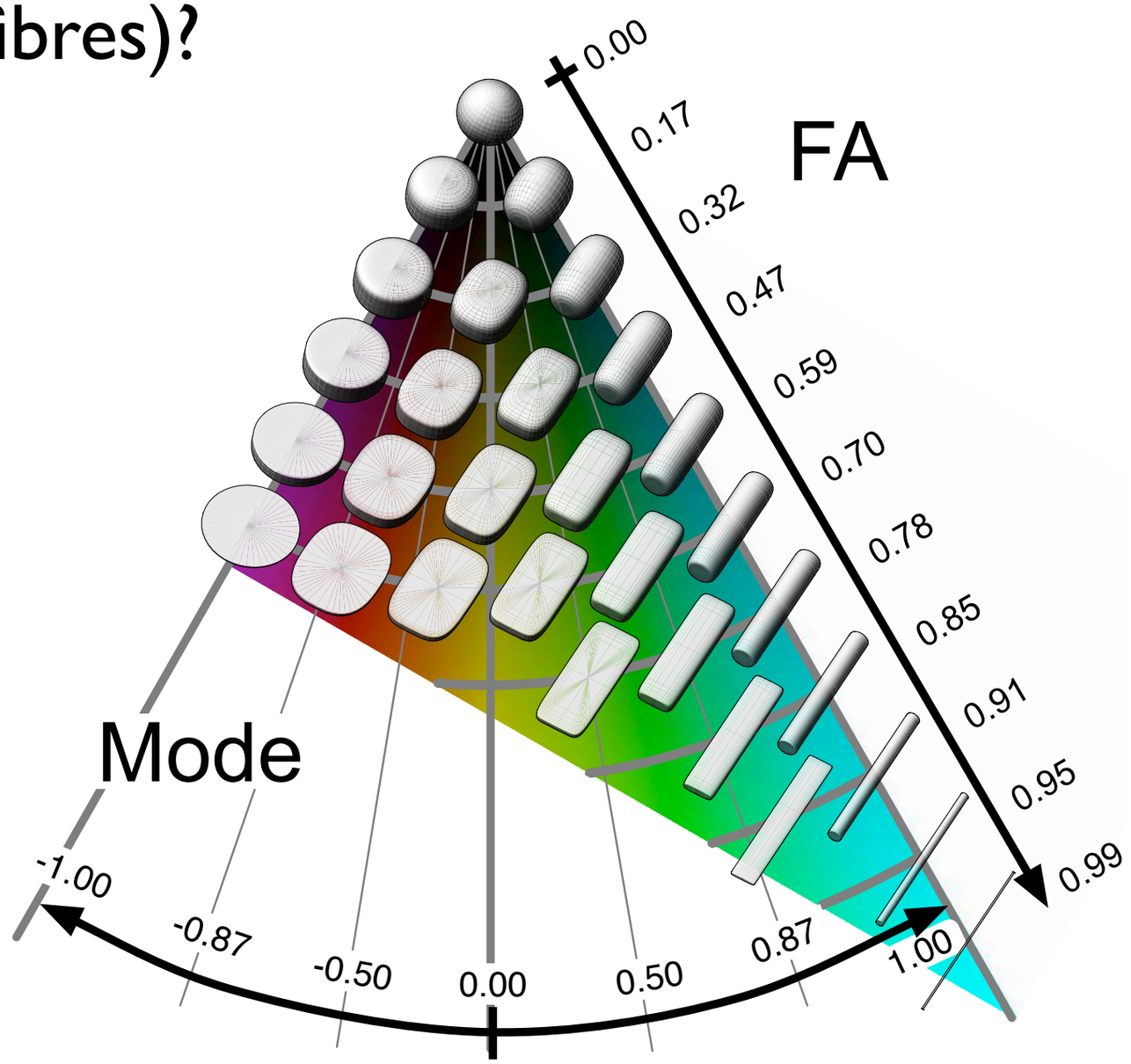


FA=0.8



Orthogonal Tensor Invariants (Kindlmann, TMI 2007)

- Nice to have 3 orthogonal (independent) tensor-derived measures: MD, FA & "Mode"
- Mode: is the tensor tubular (one strong fibre) or flat-cylindrical (two strong fibres)?



VBM-style Analysis of FA

- VBM [Ashburner 2000, Good 2001]
- Align all subjects' data to standard space
- Segment -> grey matter segmentation
- Smooth GM
- Do voxelwise stats (e.g. controls-patients)

- VBM on FA [Rugg-Gunn 2001, Büchel 2004, Simon 2005]
- Like VBM but no segmentation needed

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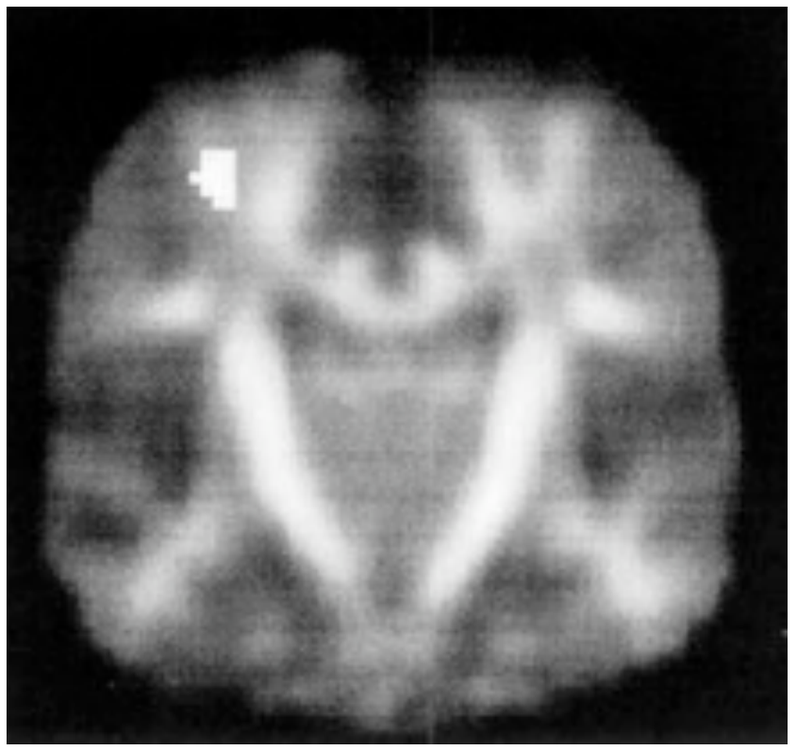
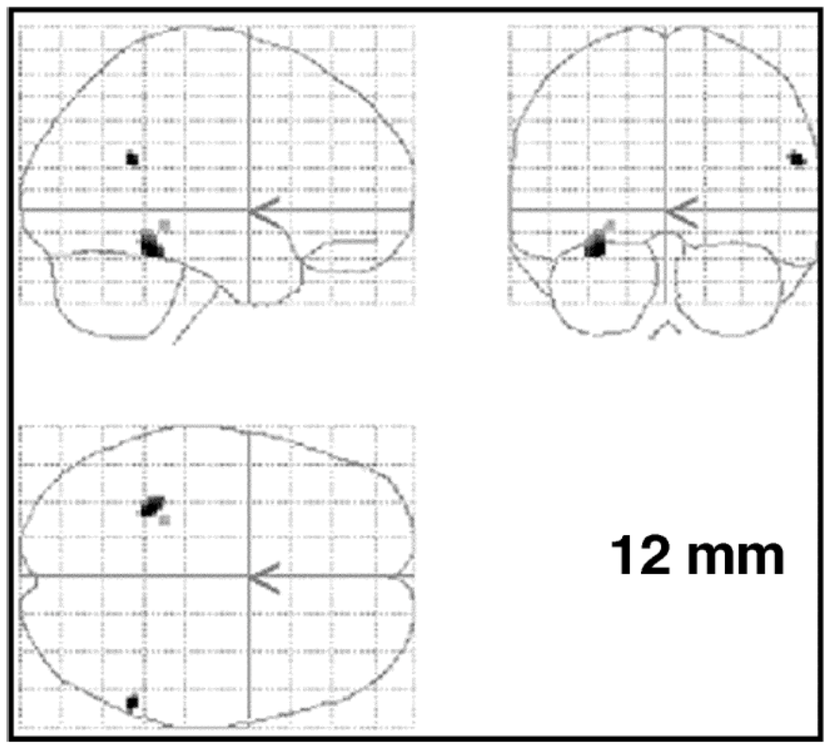


Büchel 2004

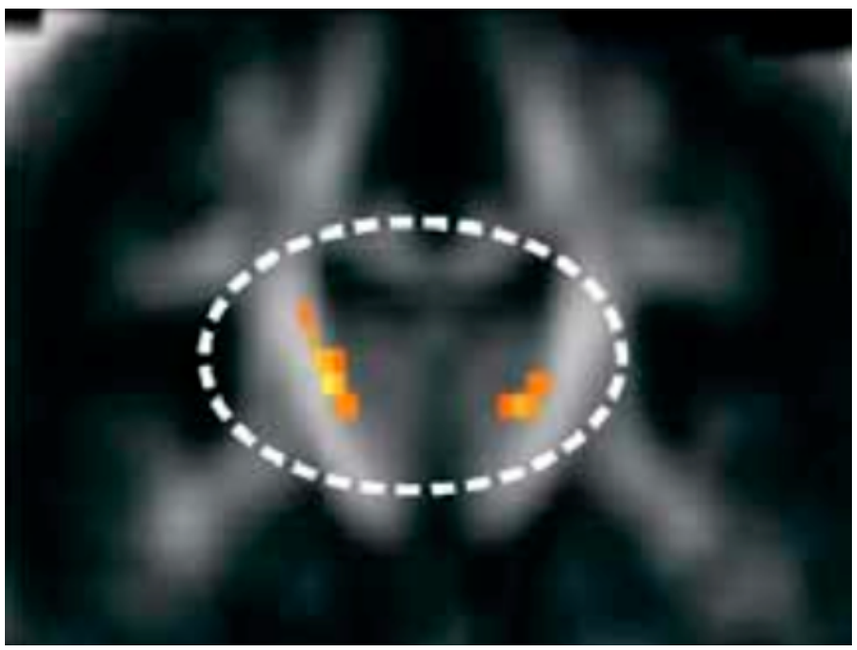
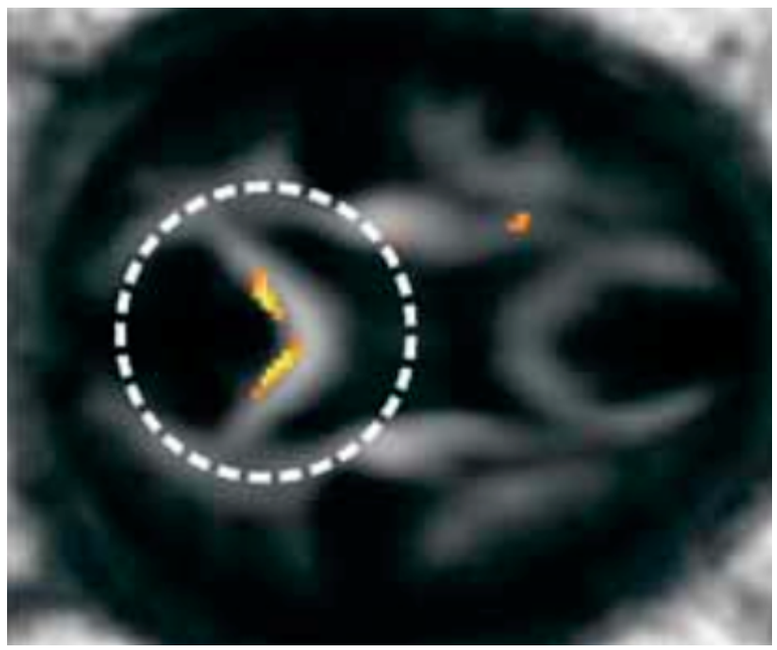
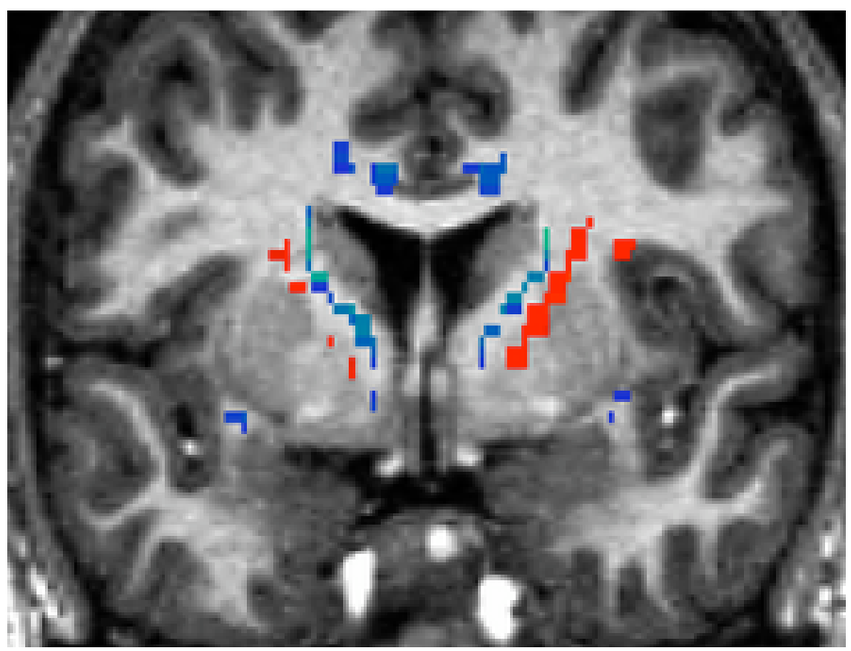


Jones 2005

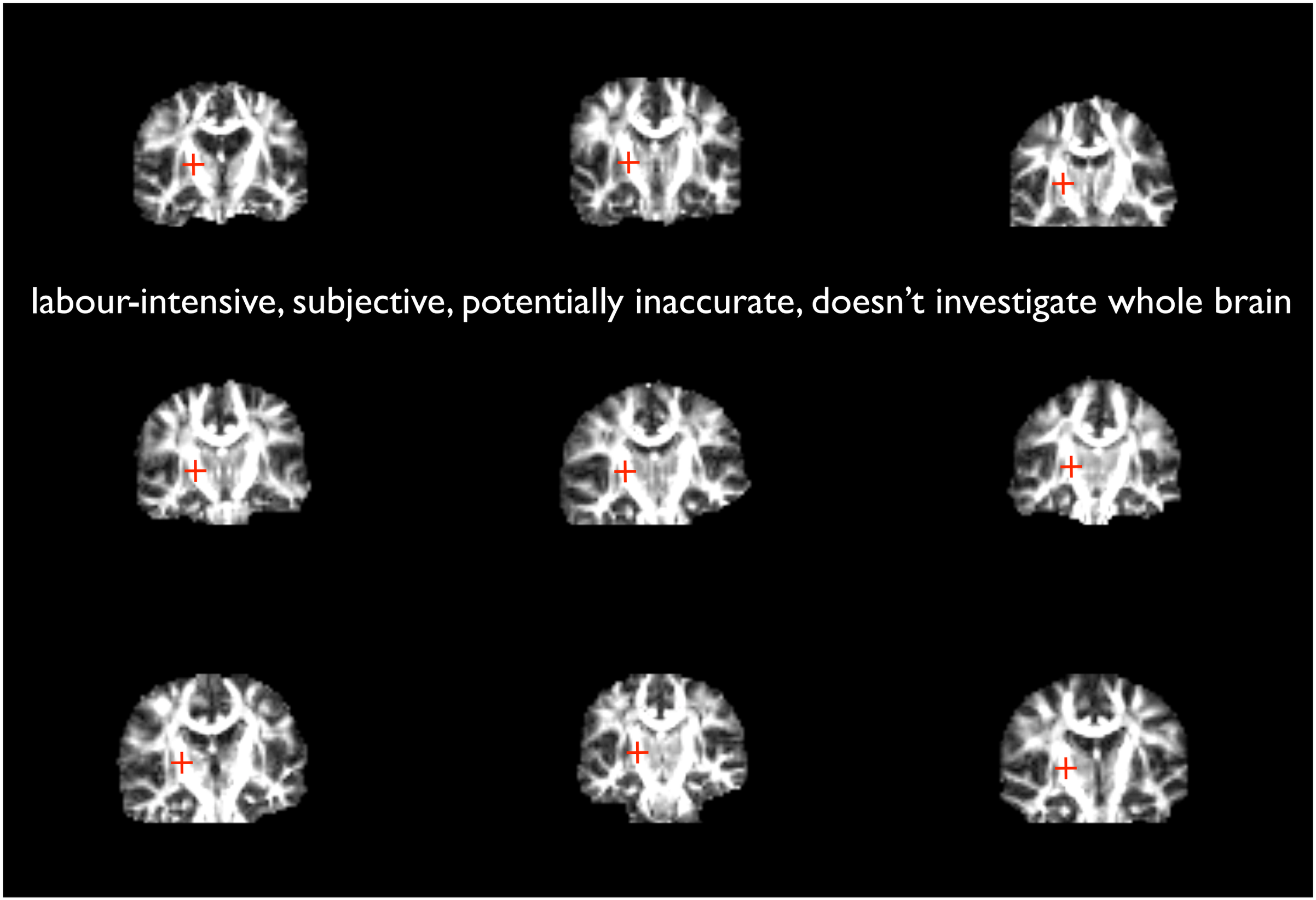
VBM-style Analysis of FA

- Strengths
  - Fully automated & quick
  - Investigates whole brain

- Problems [Bookstein 2001, Davatzikos 2004, Jones 2005]
  - Alignment difficult; smallest systematic shifts between groups can be incorrectly interpreted as FA change
  - Needs smoothing to help with registration problems
  - No objective way to choose smoothing extent

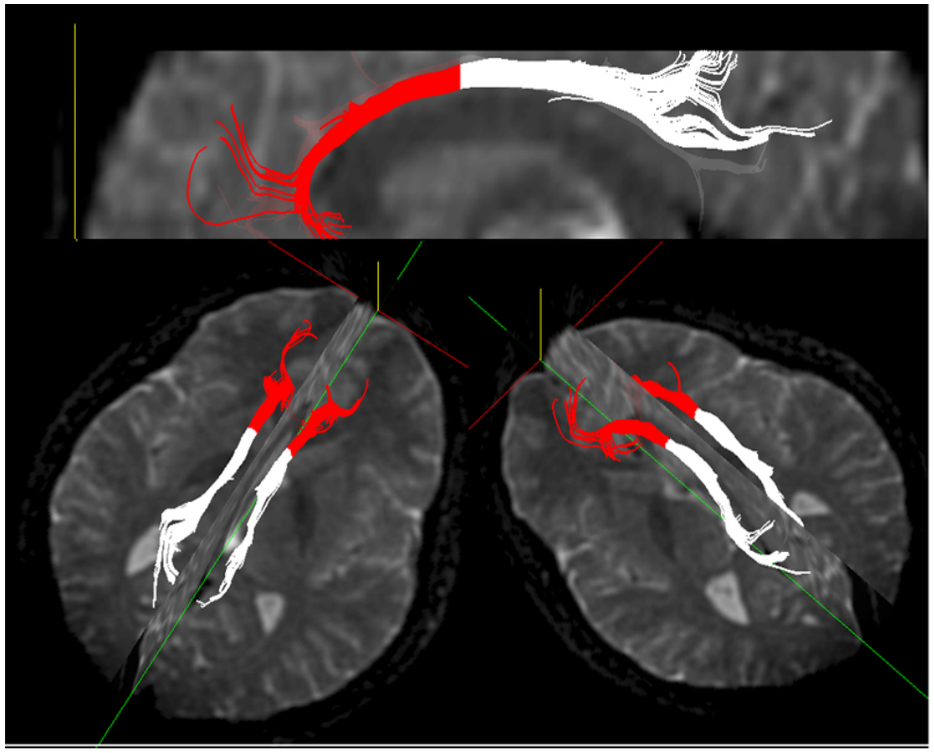




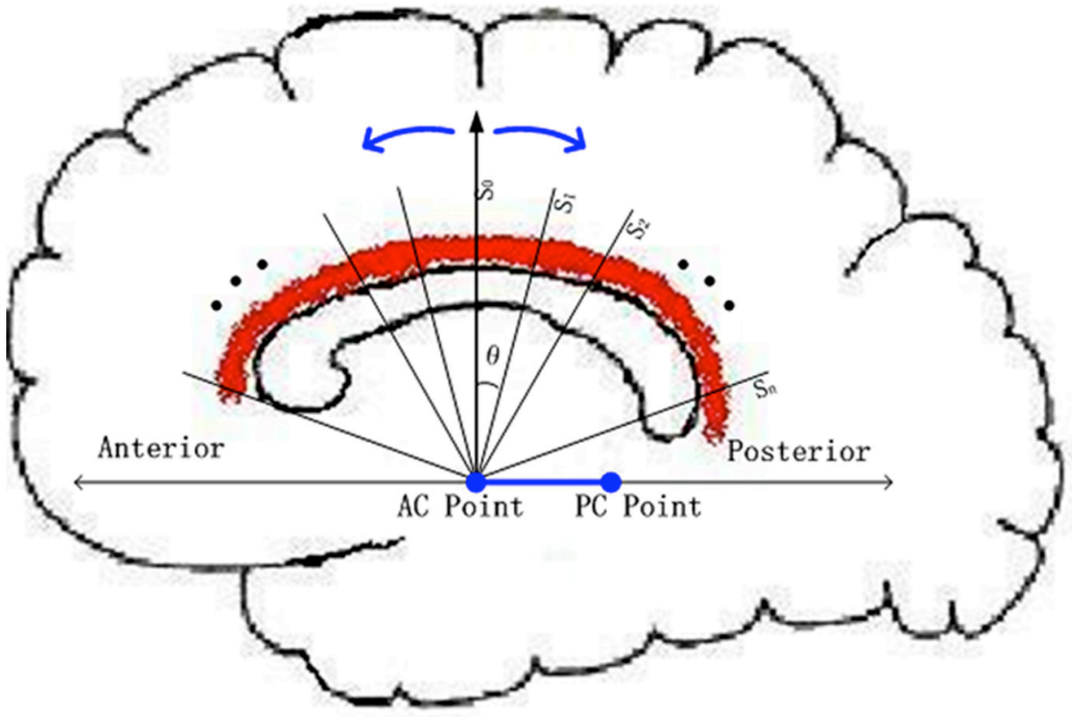
Hand-placed voxel/ROI-based FA Comparison



labour-intensive, subjective, potentially inaccurate, doesn't investigate whole brain

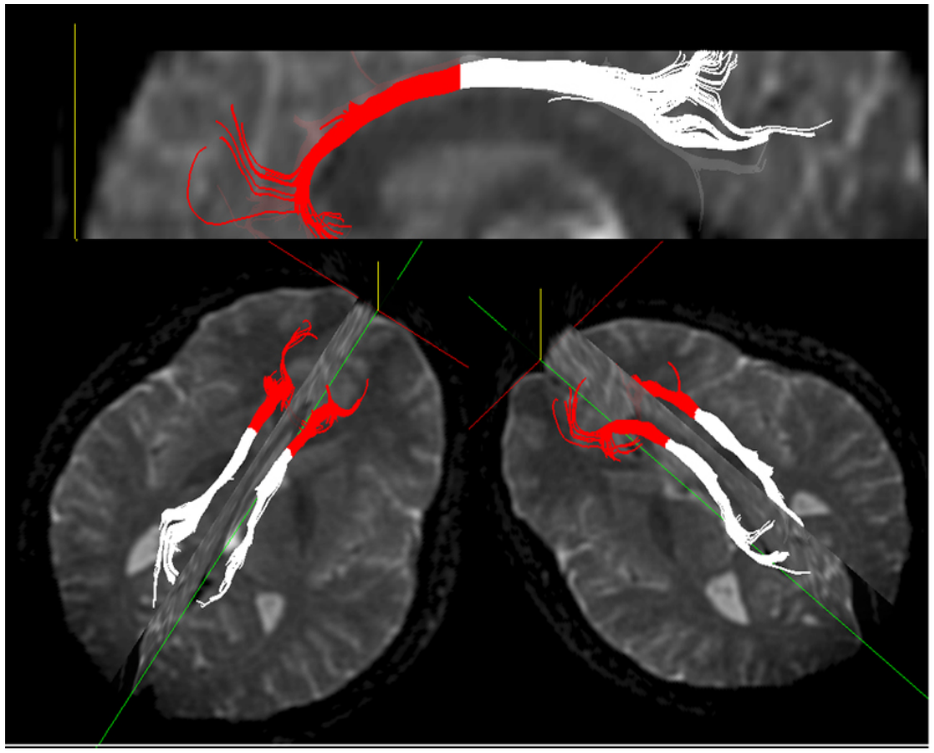
Tractography-Based FA Comparison

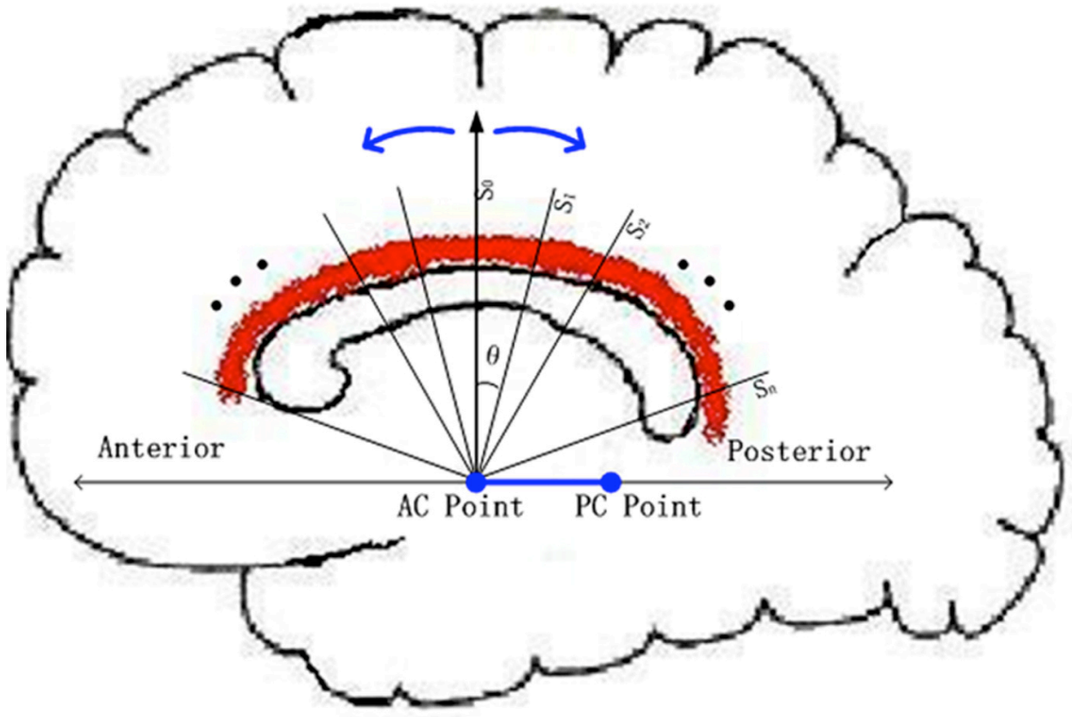




- Method [Gong 2005, Corouge 2006]
  - Define a given tract in all subjects
  - Parameterise FA along tract
  - Compare between subjects
- Strength: correspondence issue hopefully resolved
- Problems
  - Currently requires manual intervention to specify tract
  - Hence doesn't investigate whole brain
  - Projection of FA onto tract needs careful thought

Tractography-Based FA Comparison





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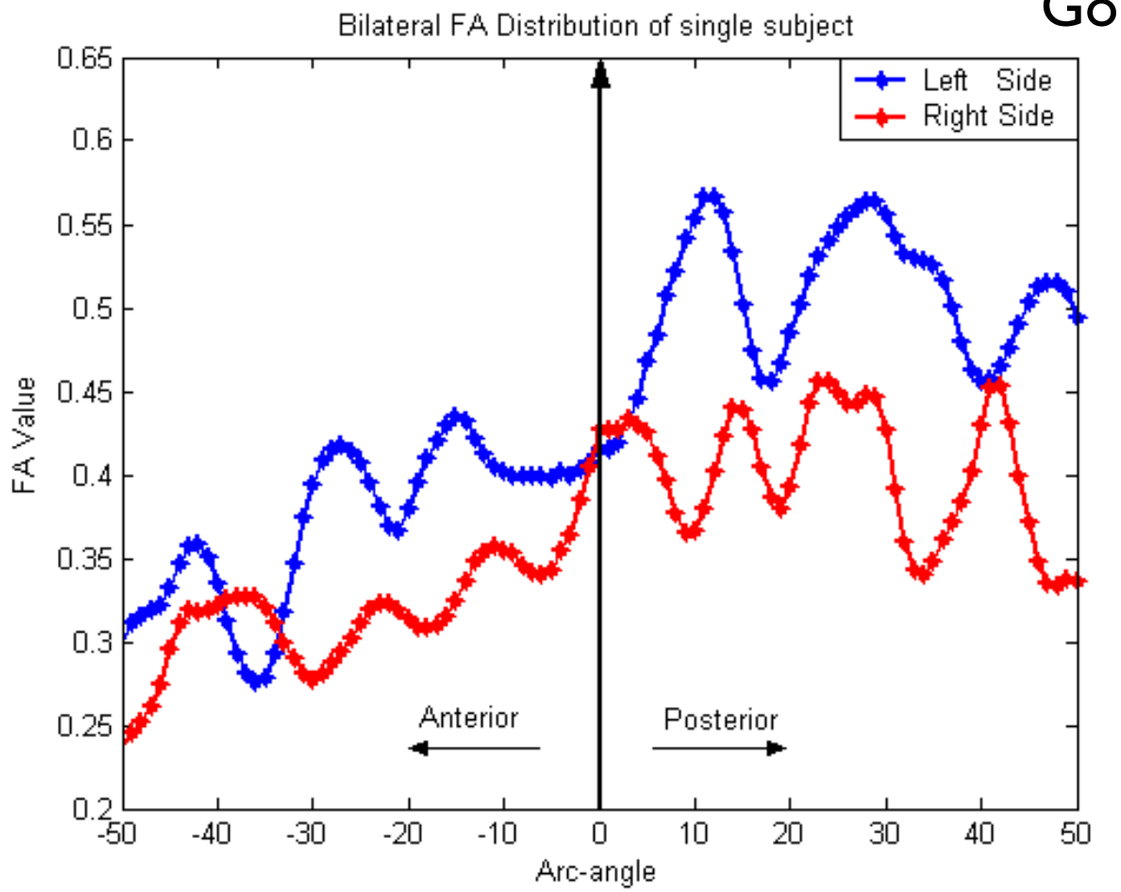
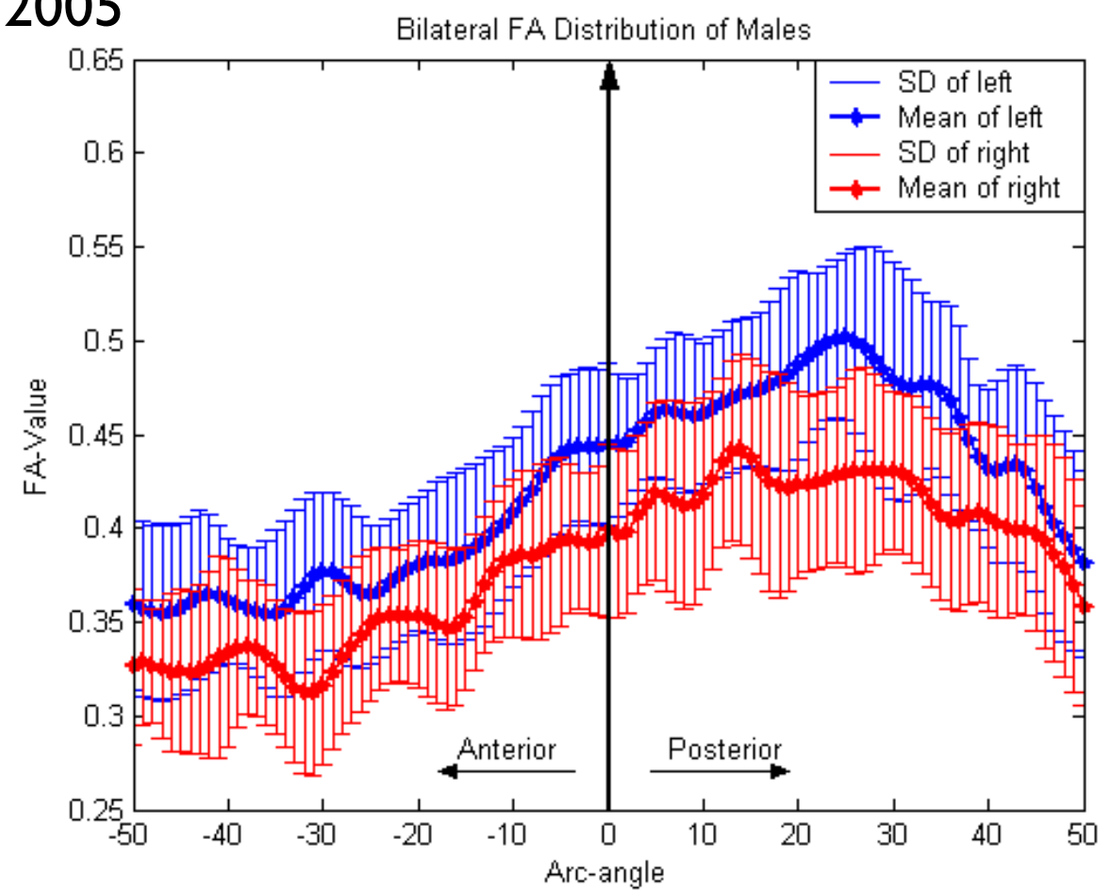




Tractography-Based FA Comparison

Yushkevich & Gee, NeuroImage 2008

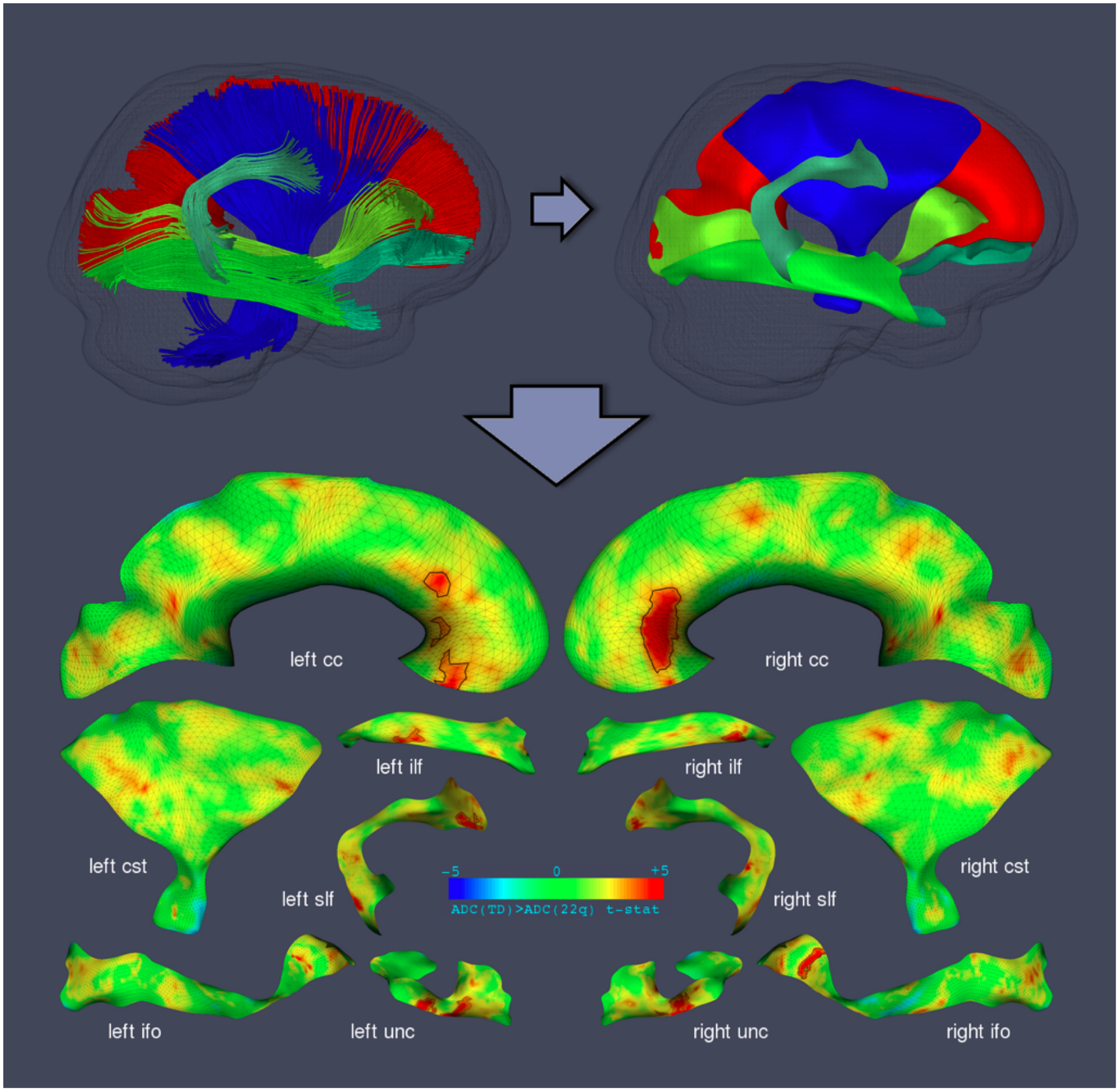
- cross-subject tensor averaging

➡ standard-space tractography (6 major fasciculi)

➡ medial surfaces

➡ project MD onto medial surface

➡ cross-subject stats



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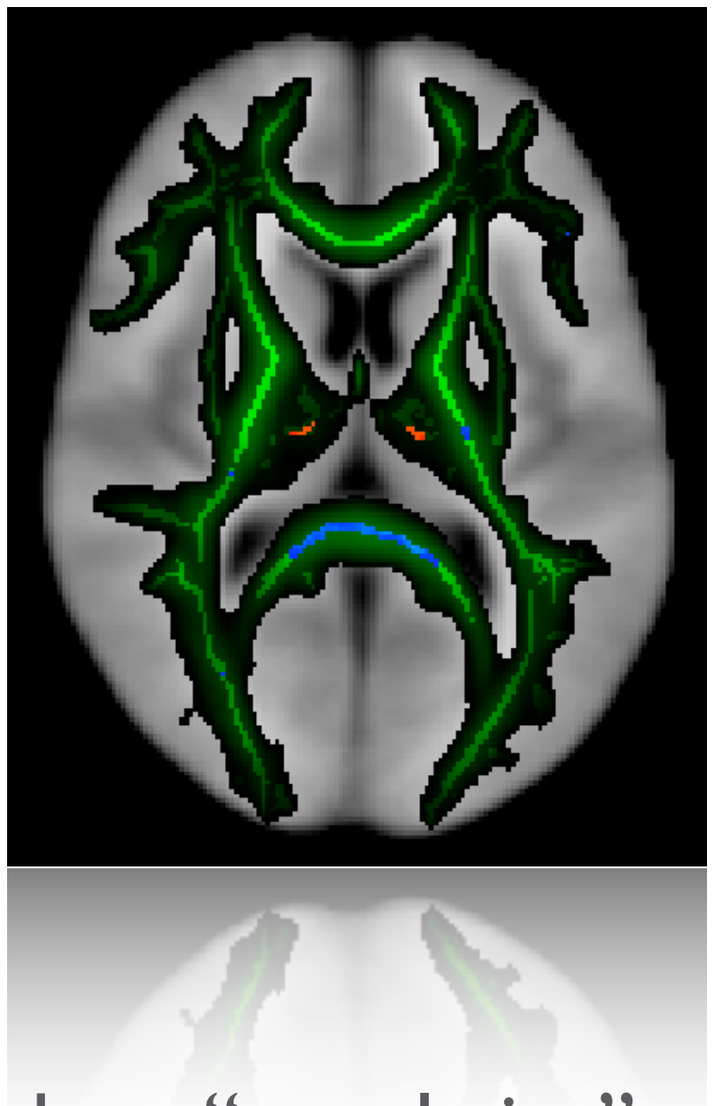

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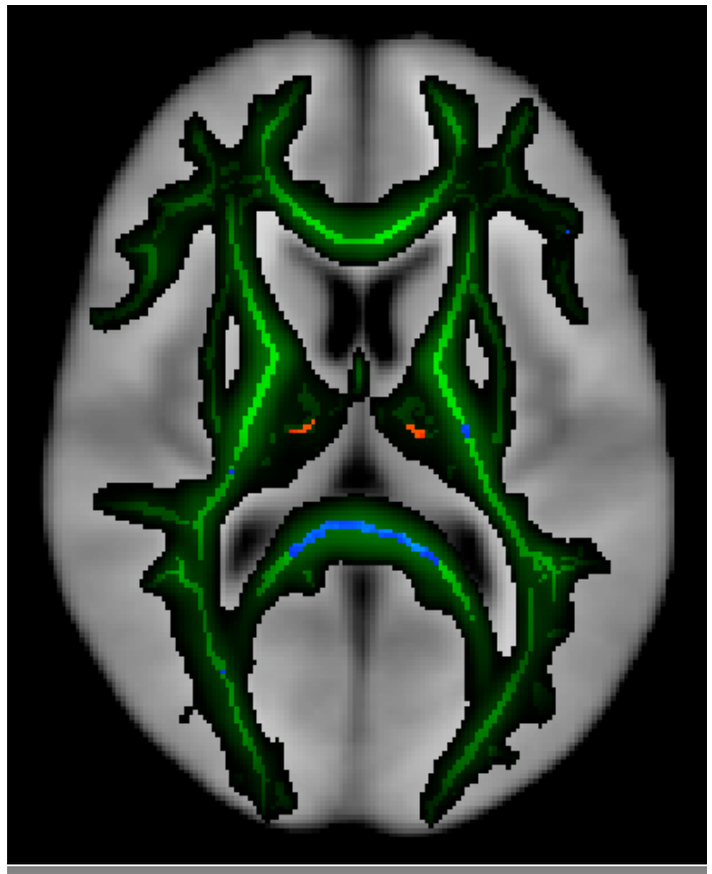

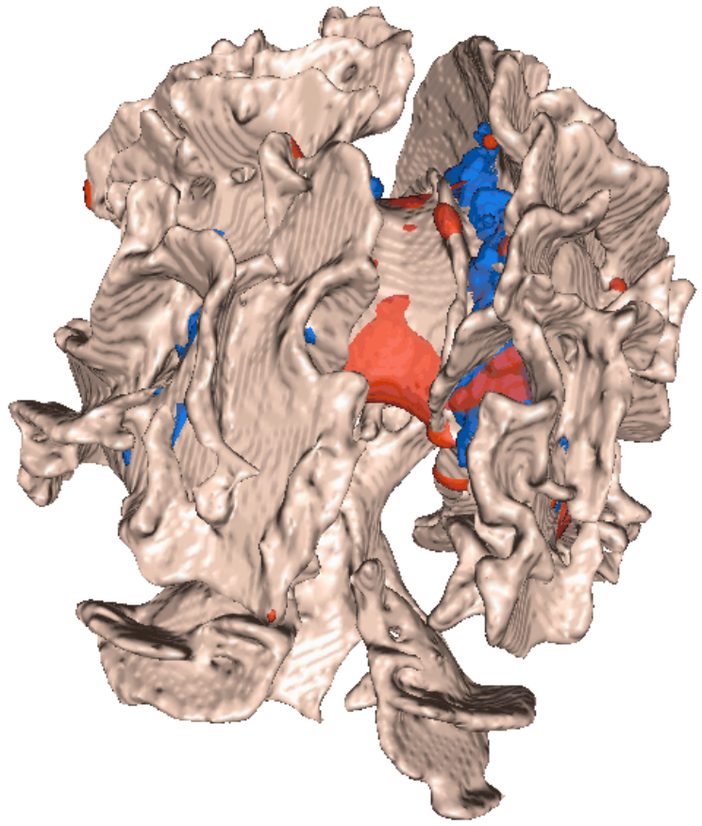

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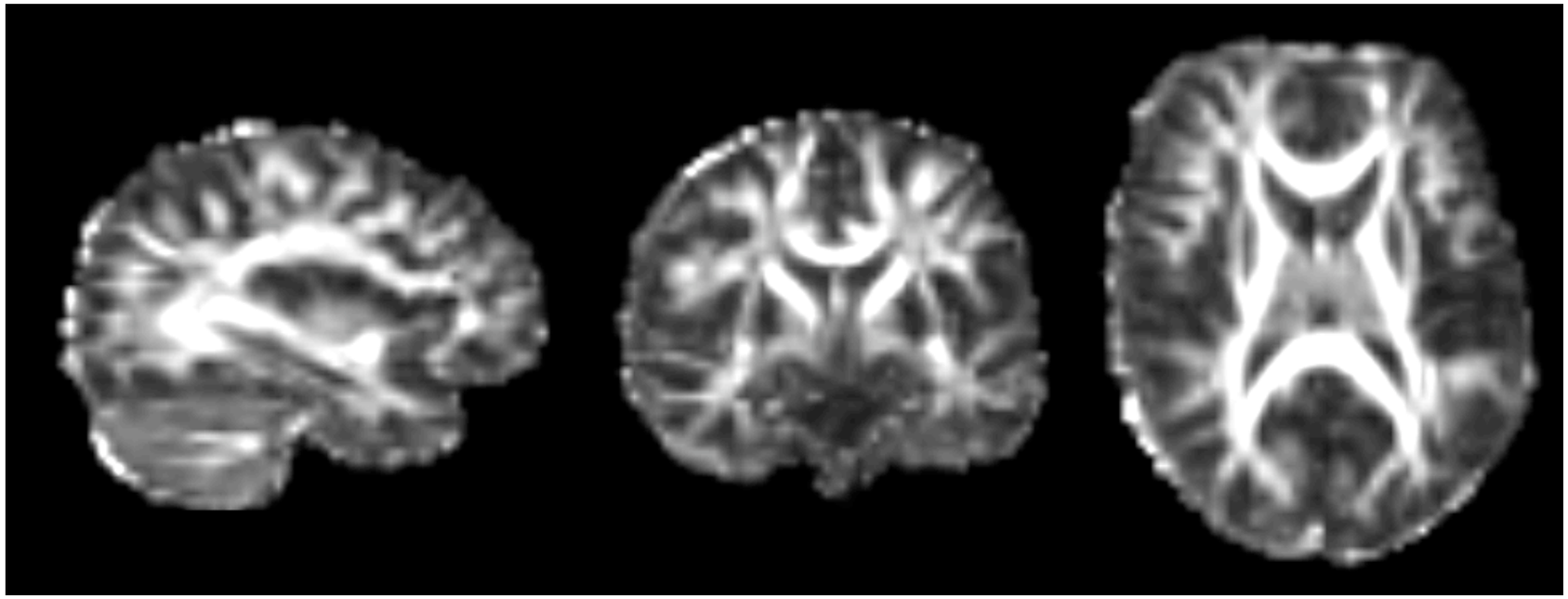
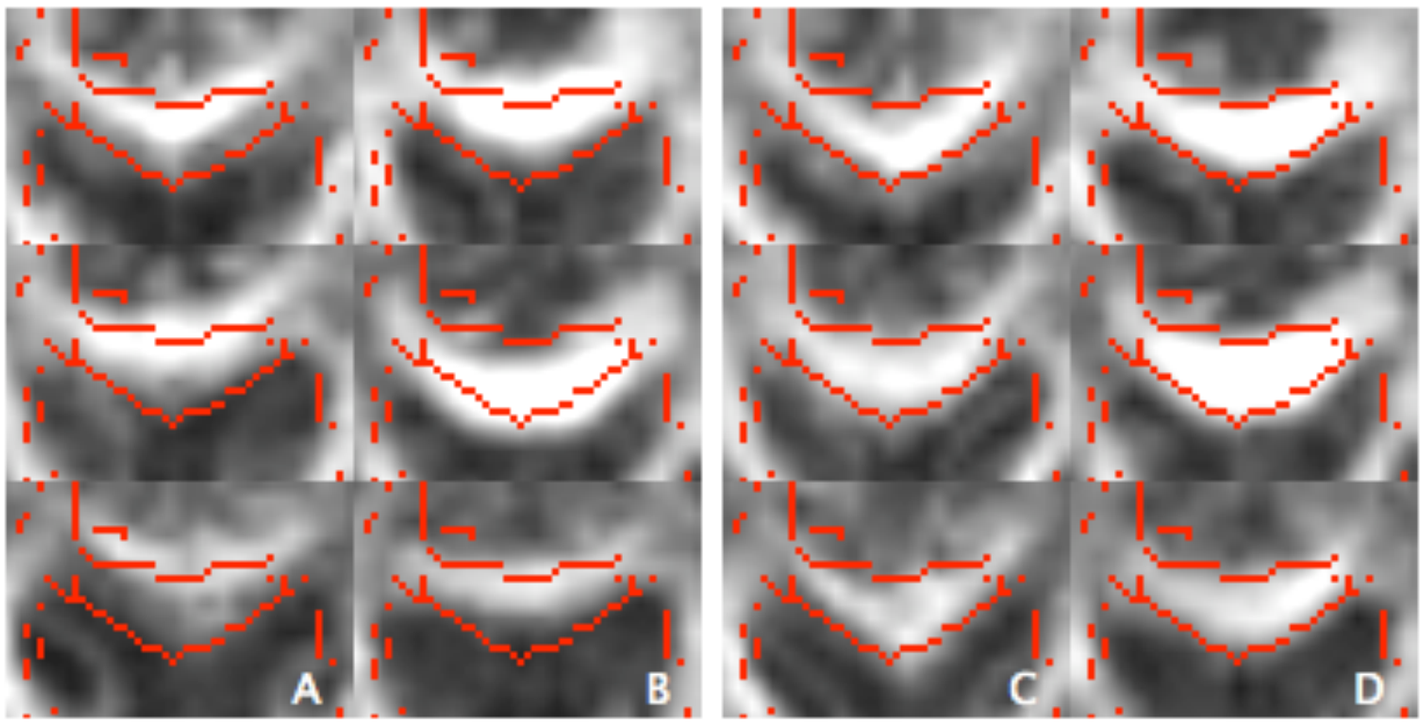
(nonlinear reg: FNIRT)





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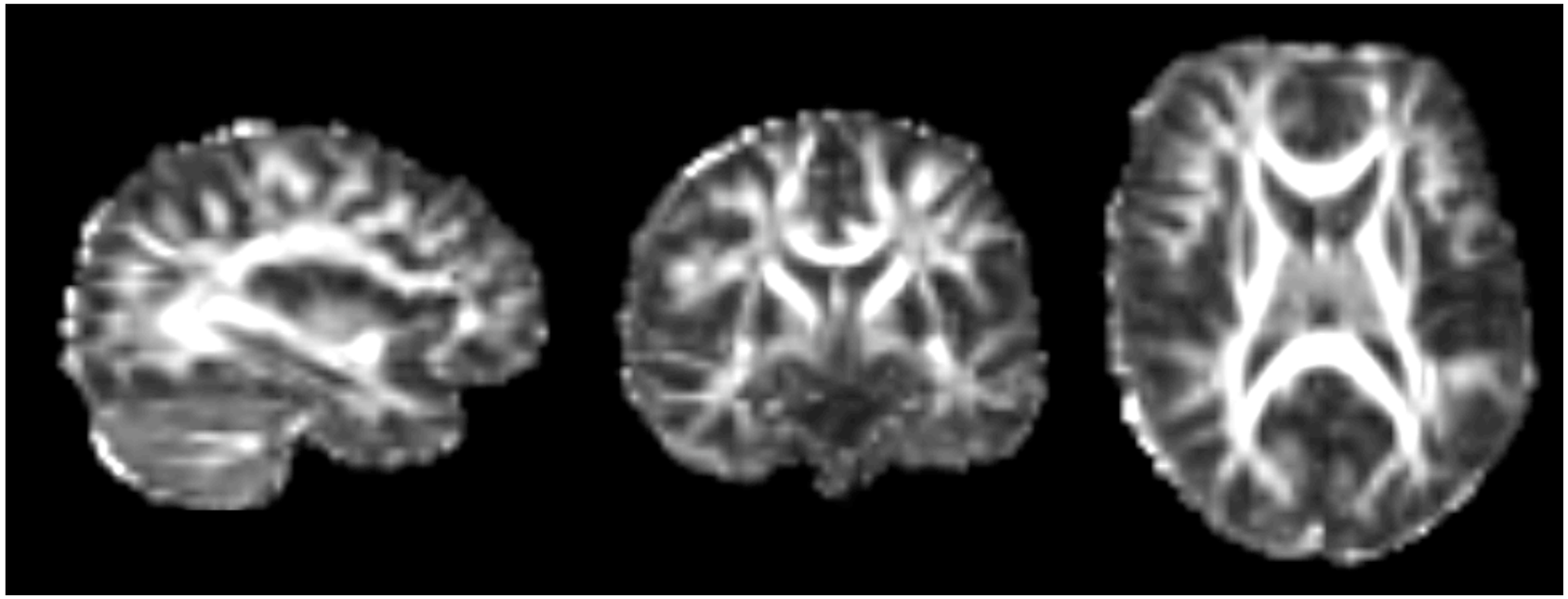
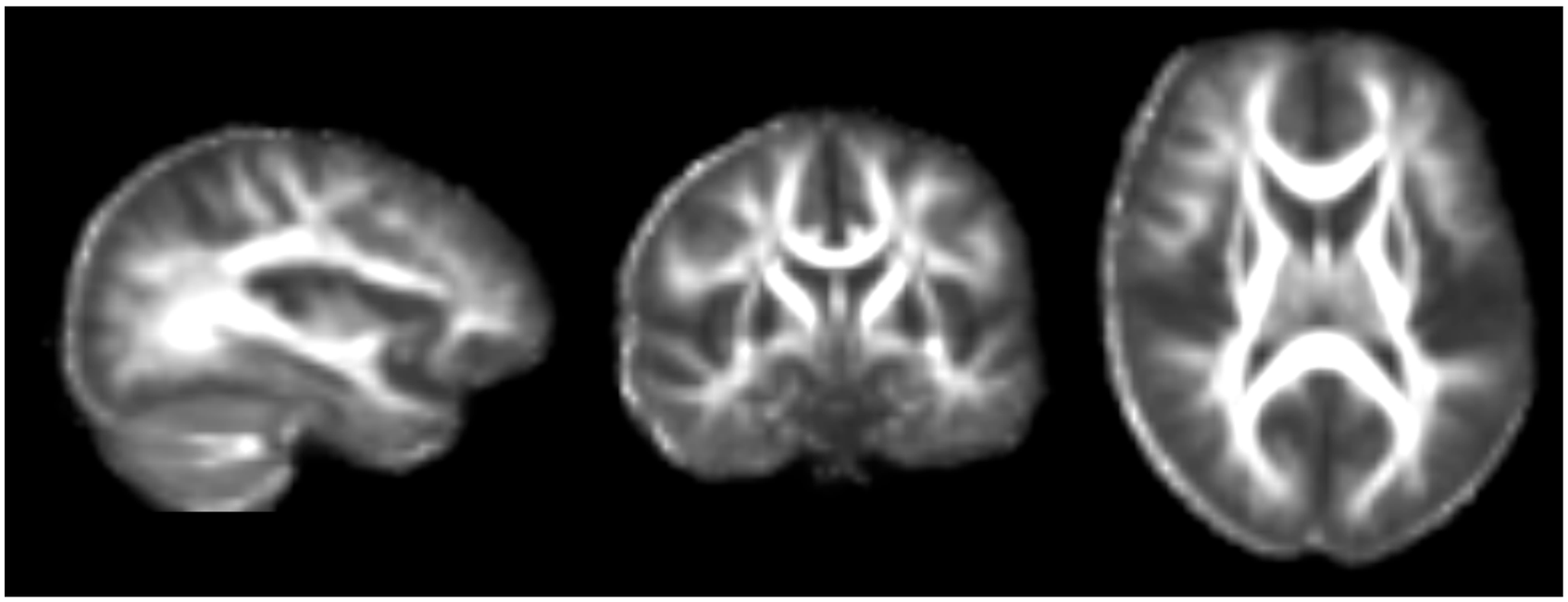


2. Create mean FA image (no smoothing)



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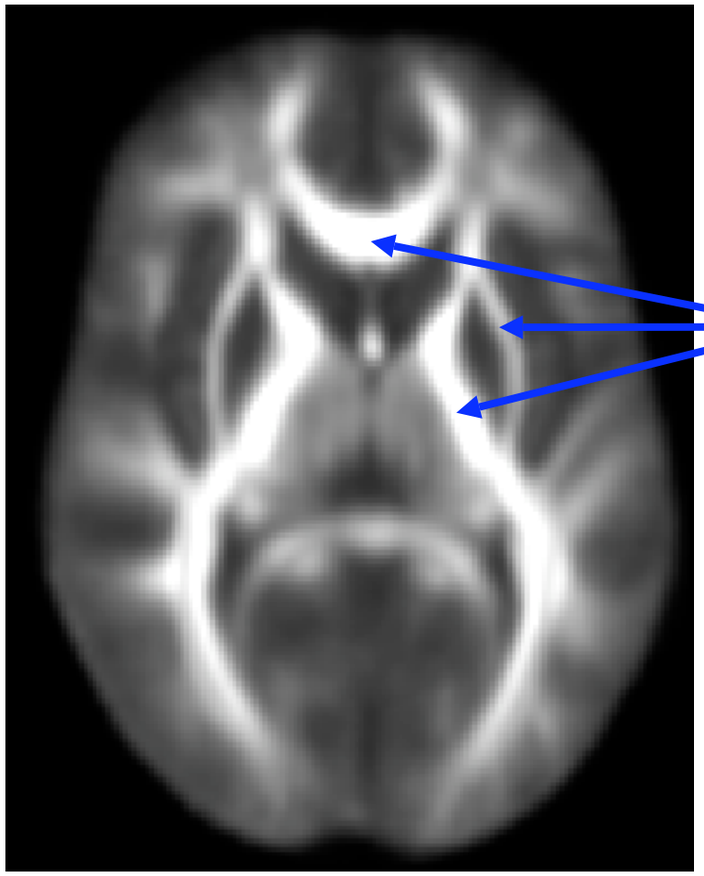

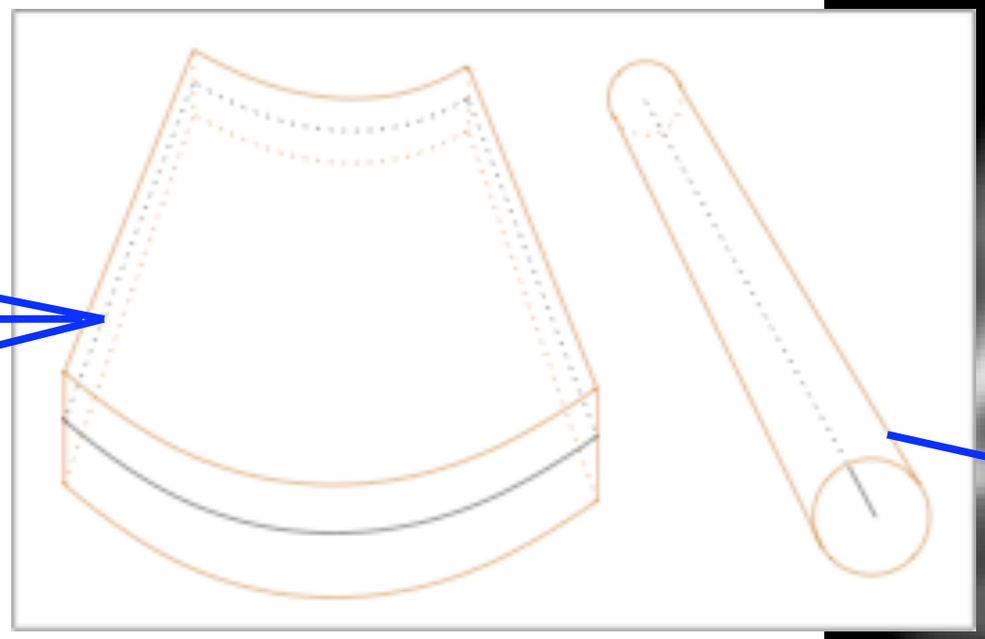

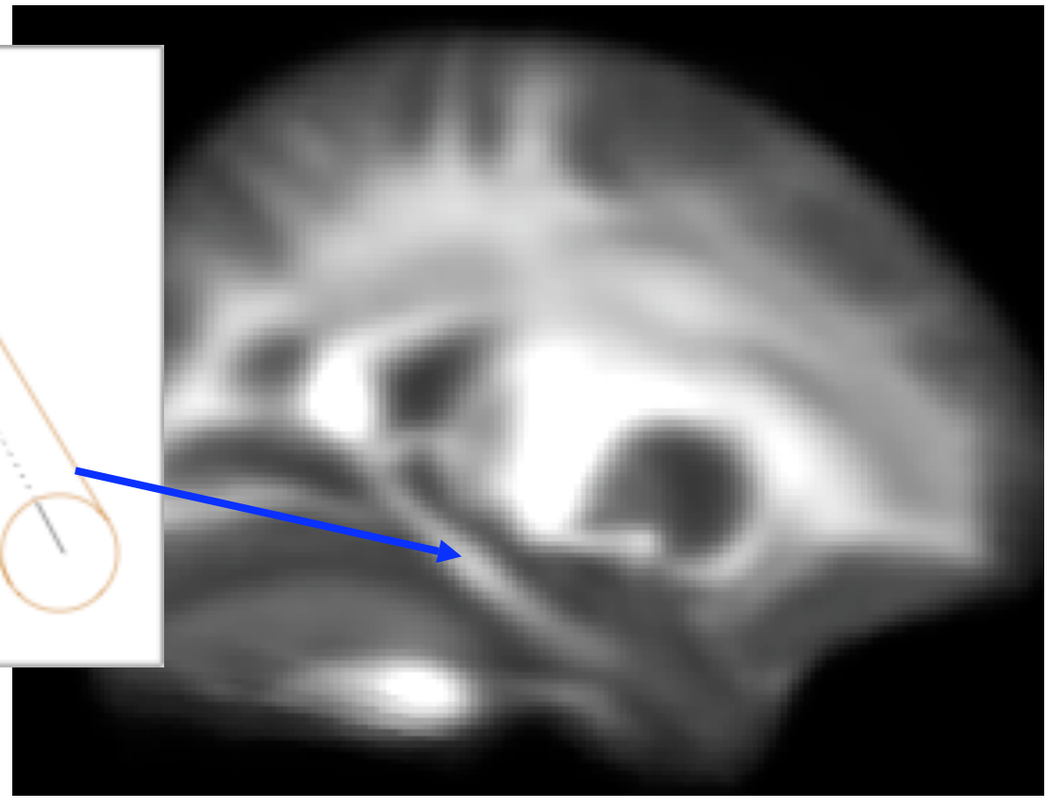

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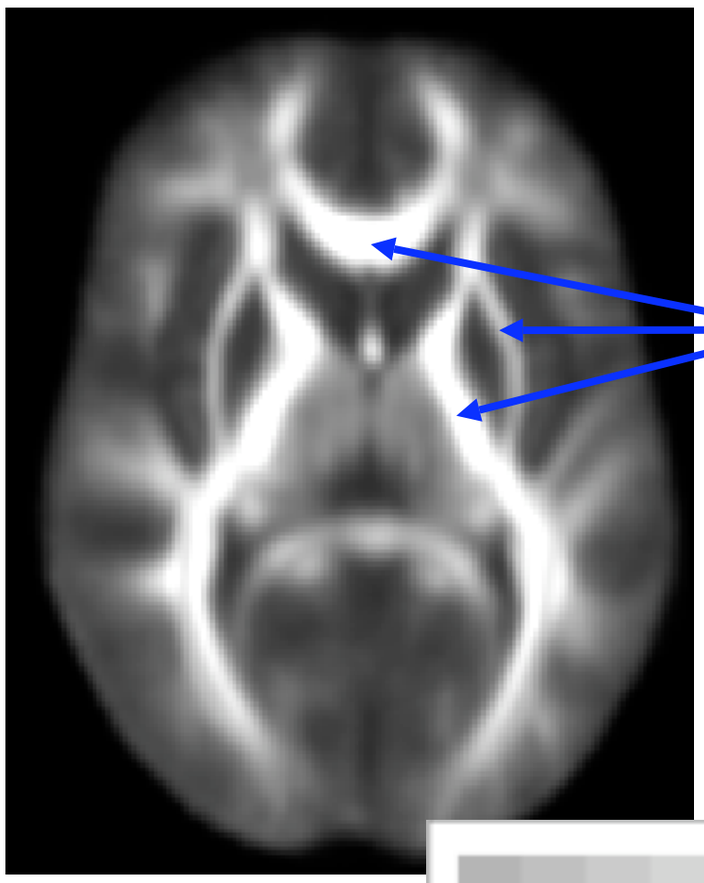
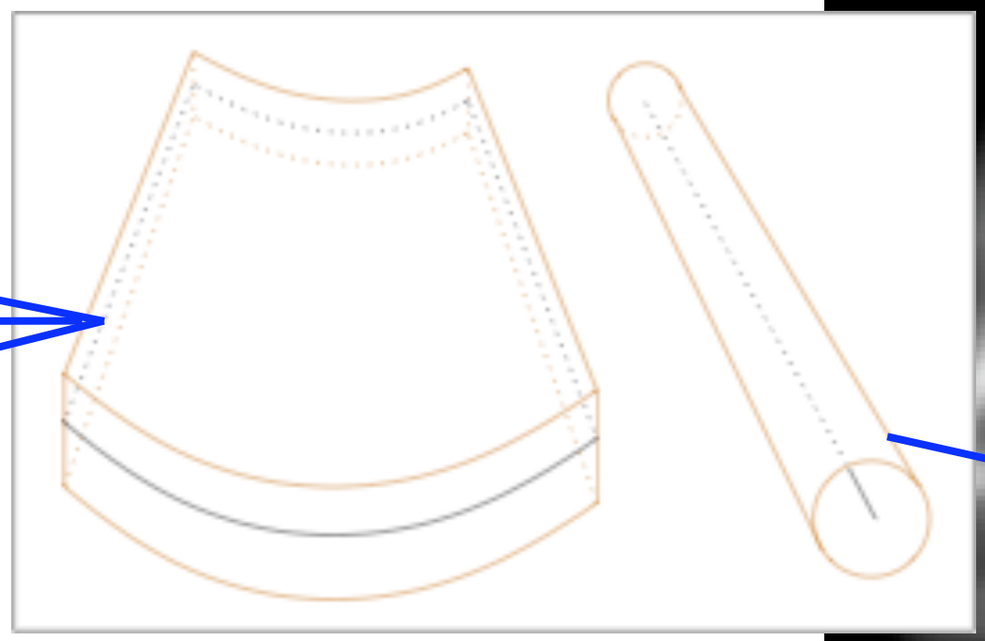
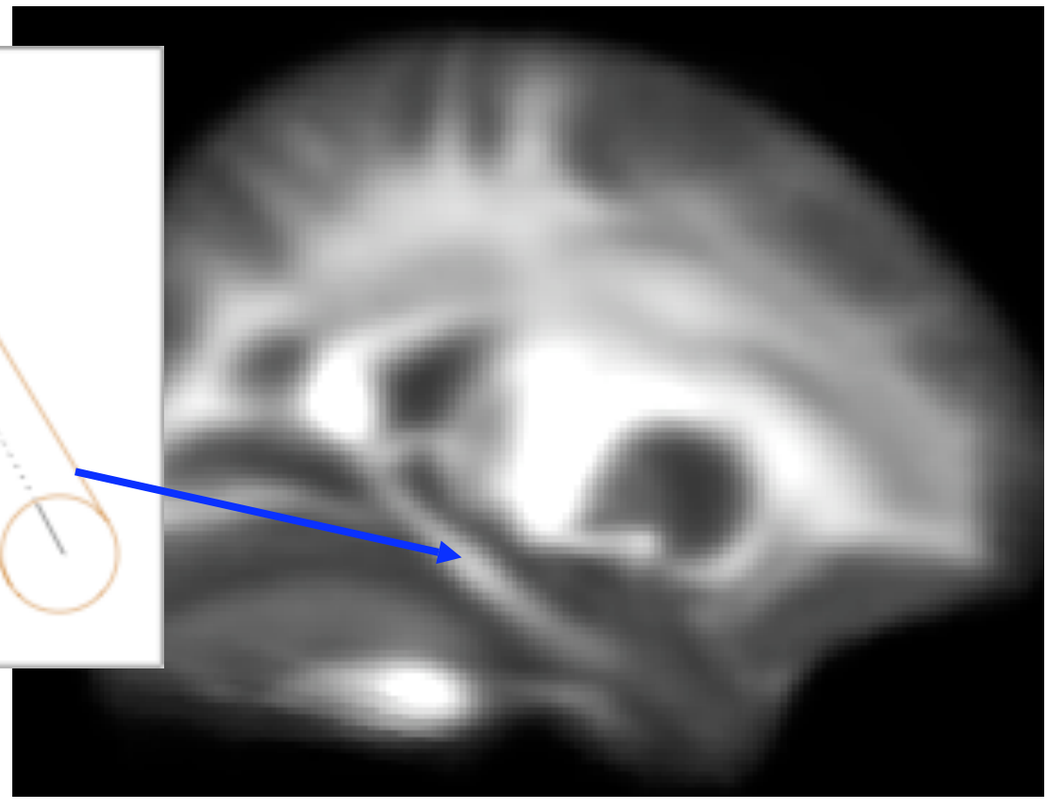
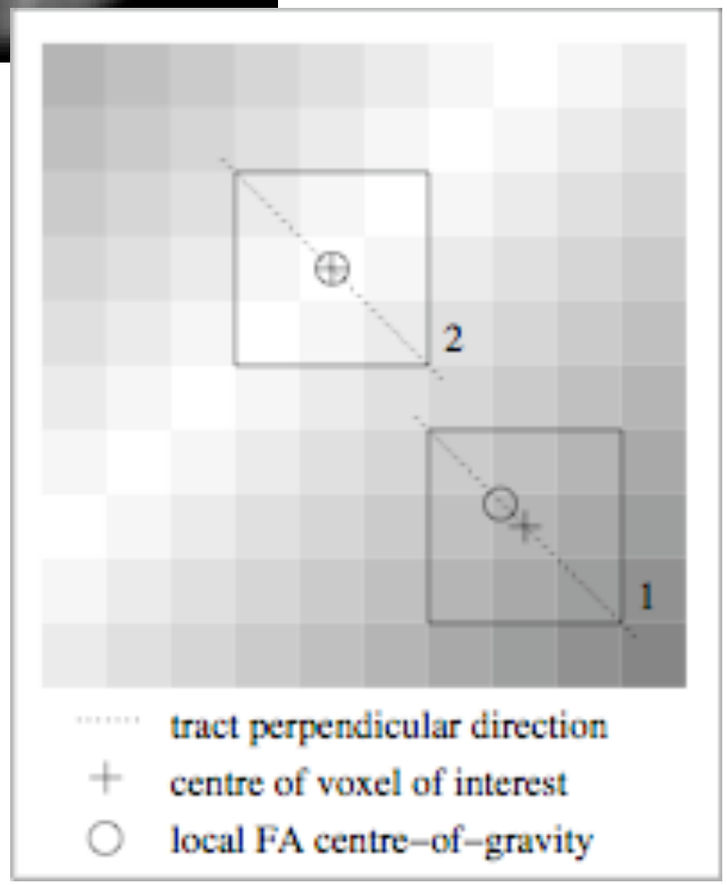


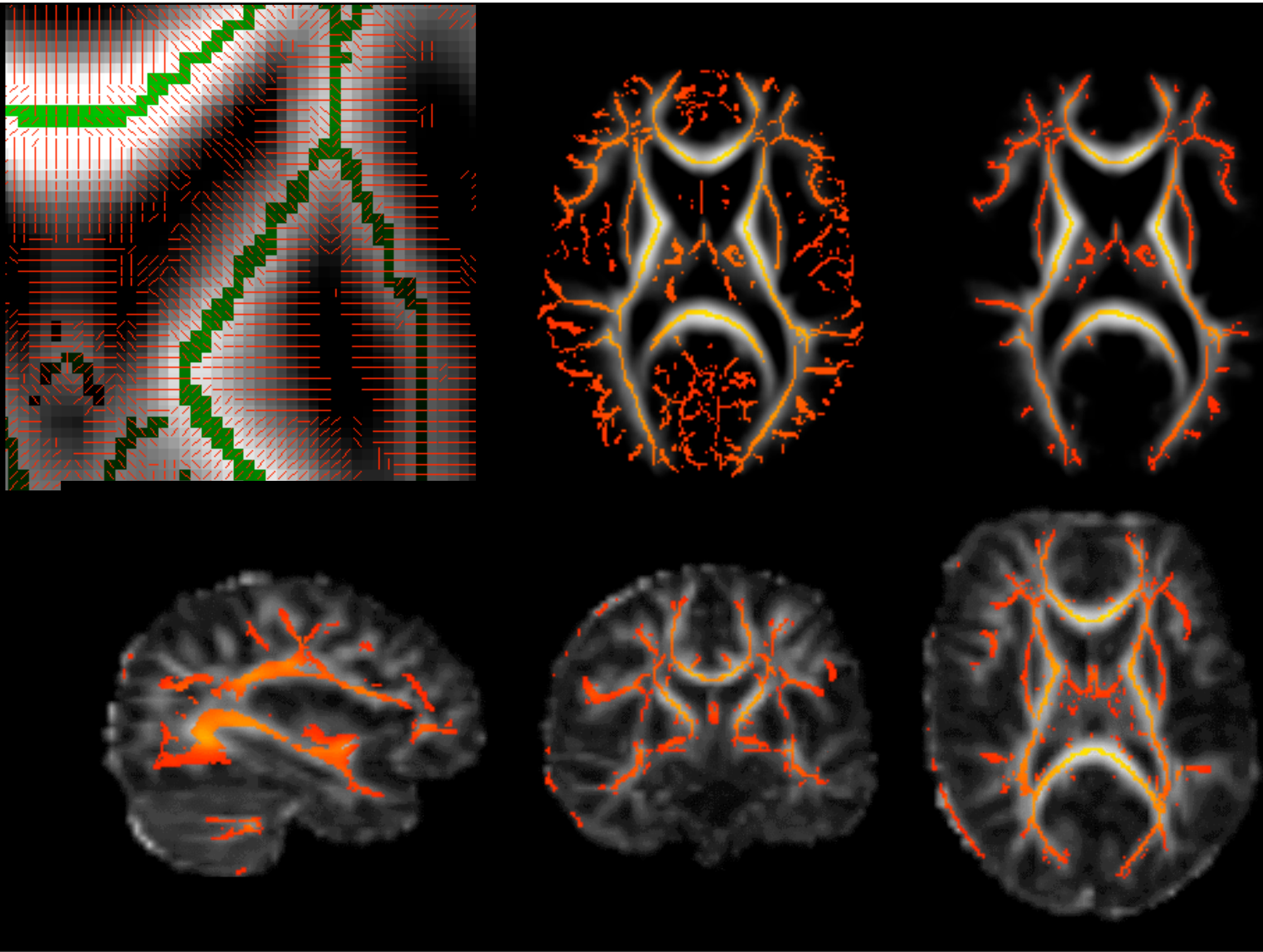






3. Threshold Mean FA Skeleton

giving "objective" tract map



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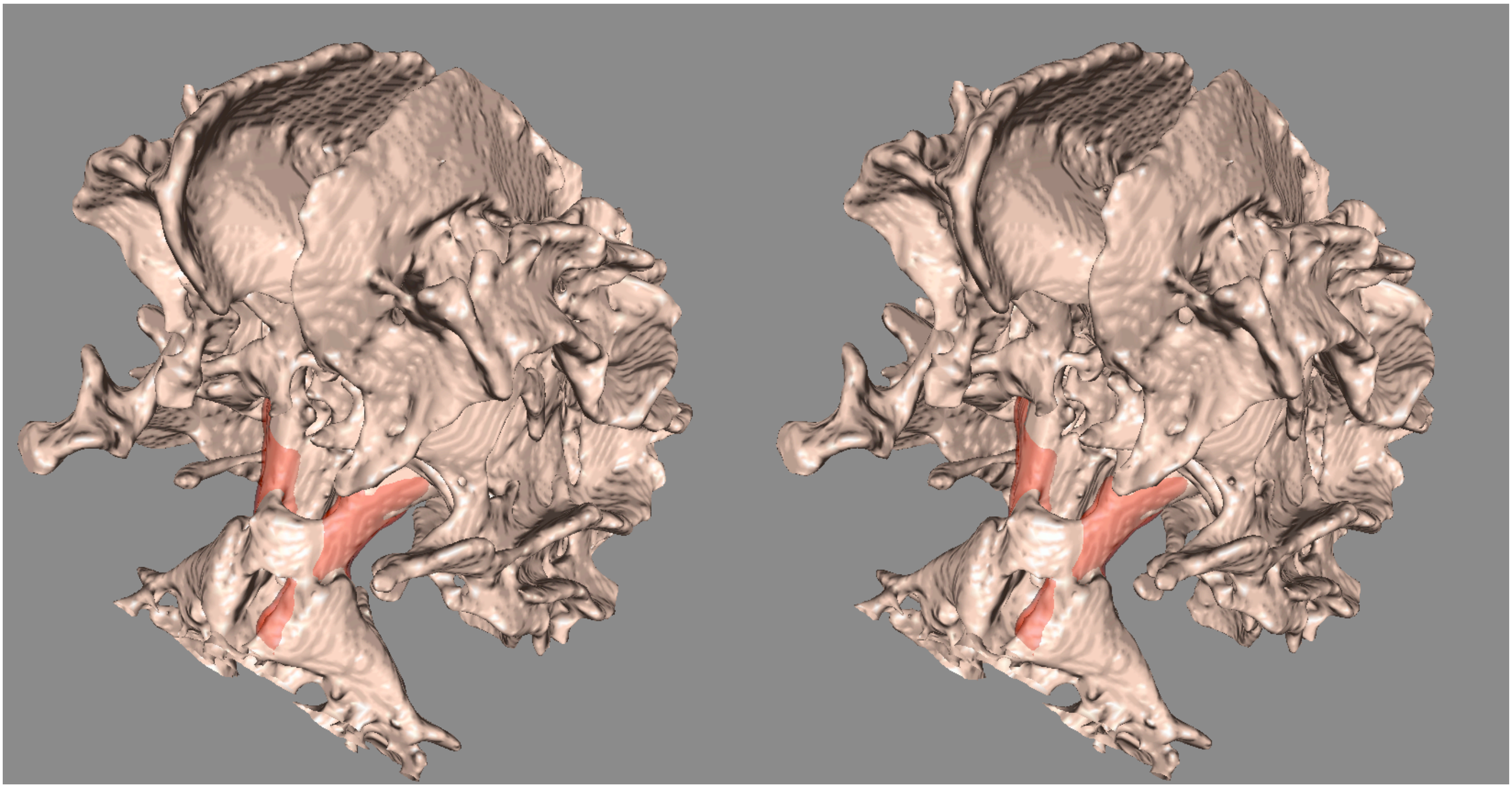

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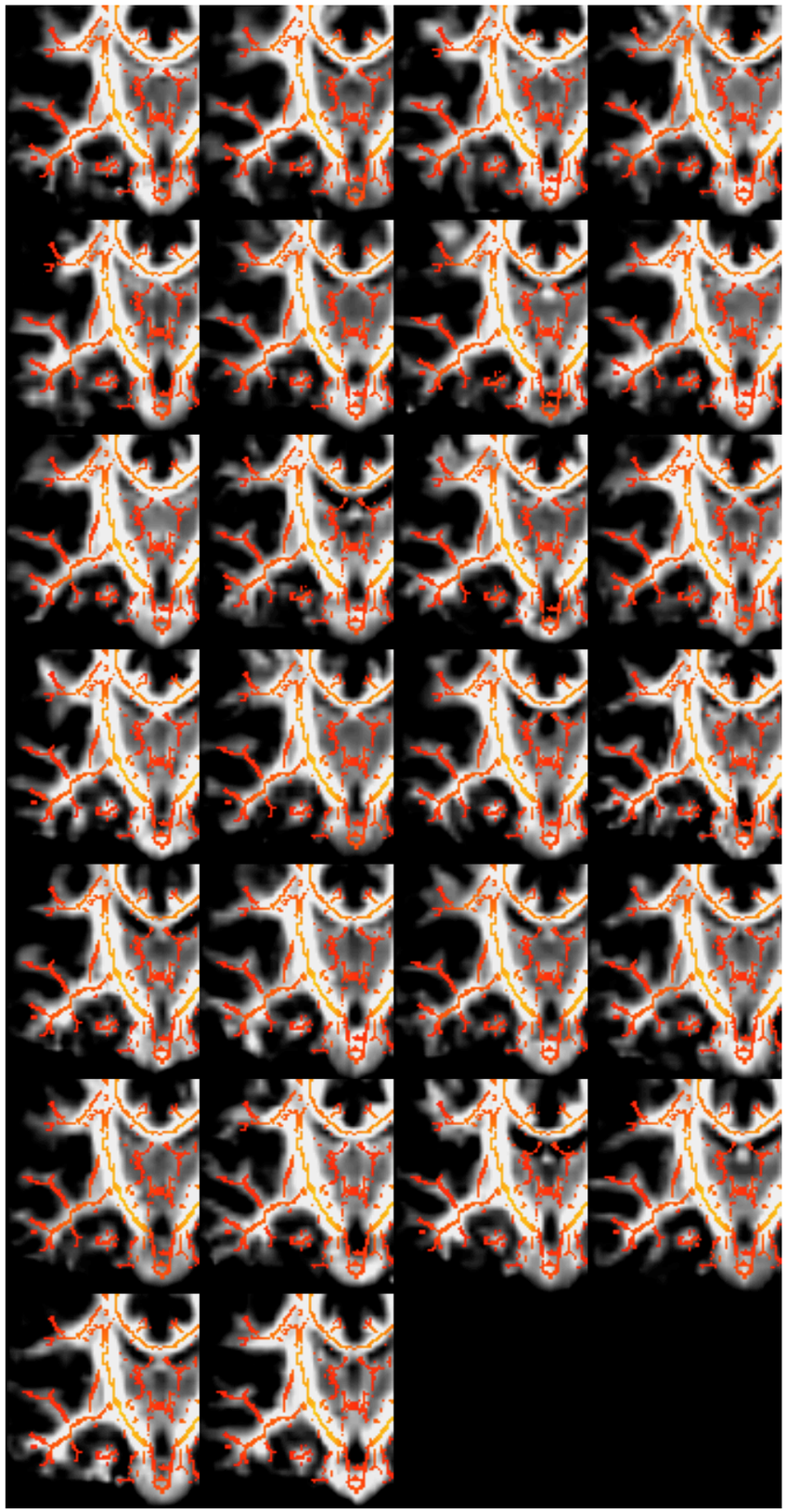
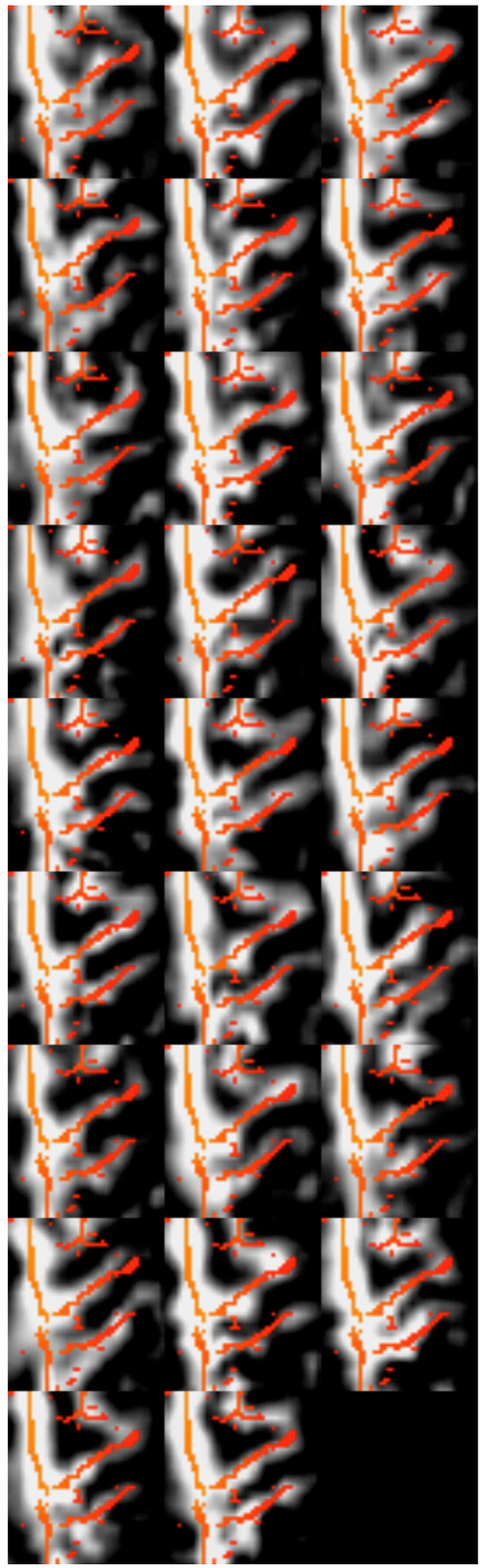
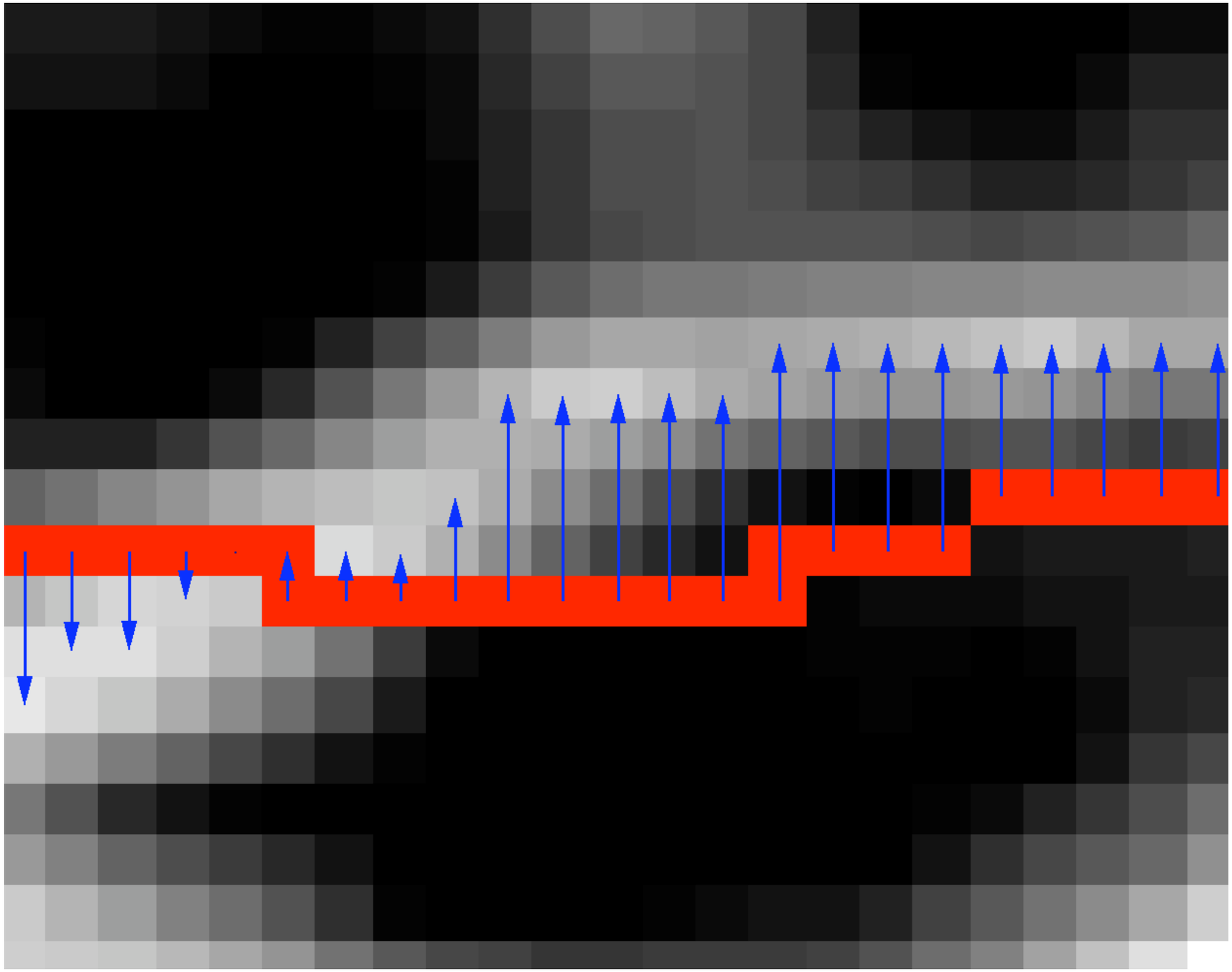




4. For each subject's warped FA, fill each point on the mean-space skeleton with nearest maximum FA value (i.e., from the centre of the subject's nearby tract)



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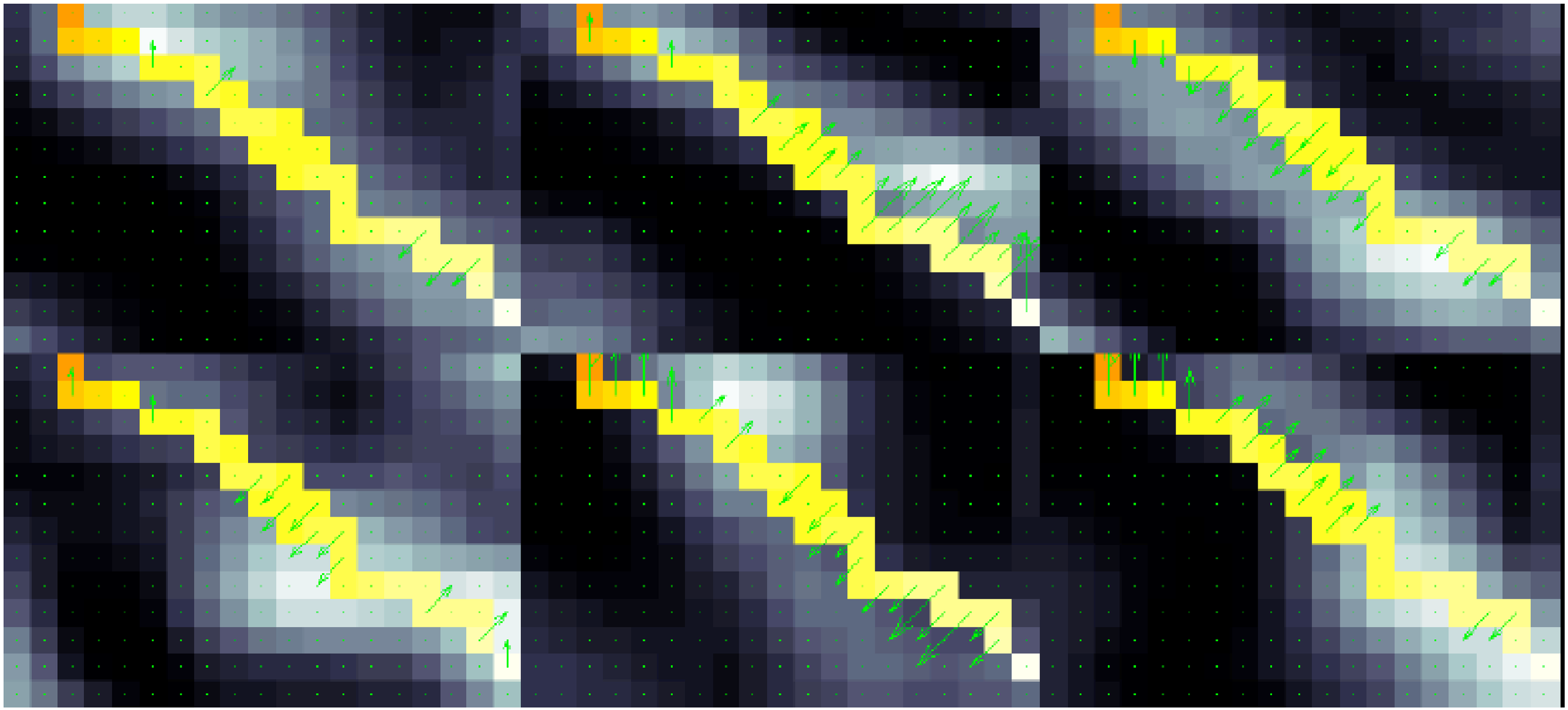


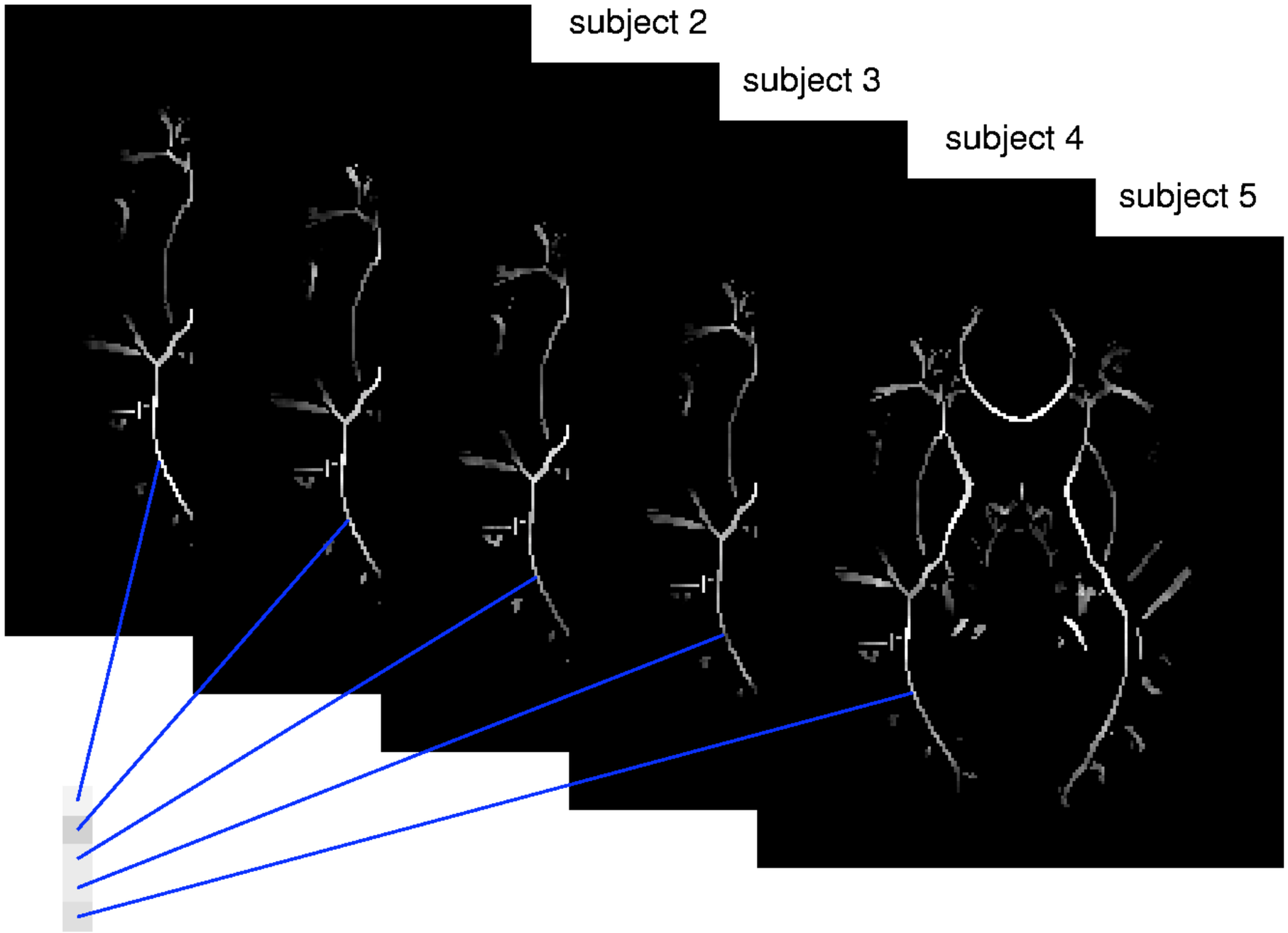
subject 1

subject 2

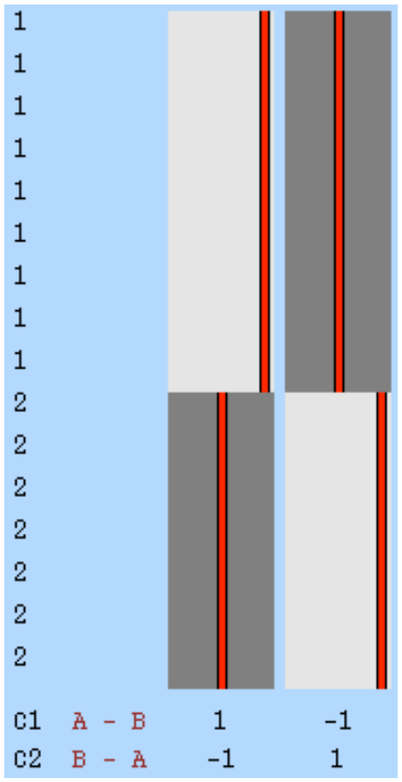
subject 3

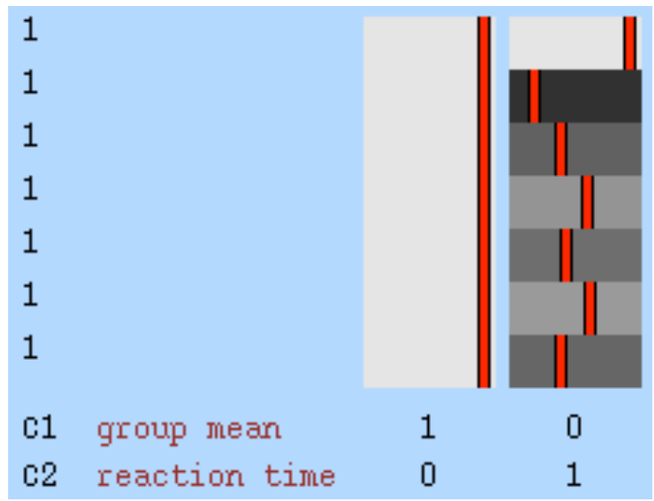
subject 4

subject 5

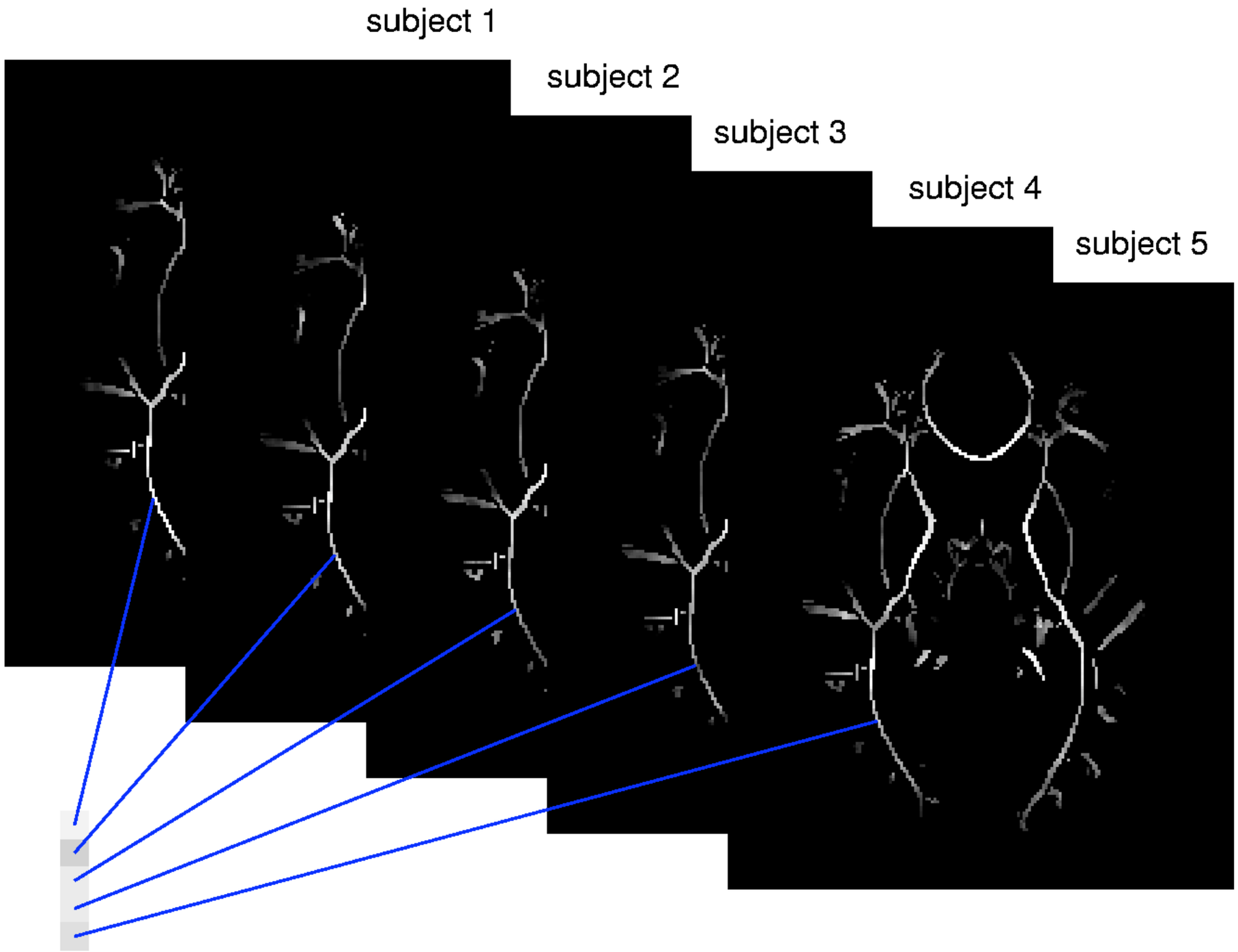


one skeleton voxel's data vector (to be fed into GLM)





5. Do cross-subject voxelwise stats on skeleton-projected FA



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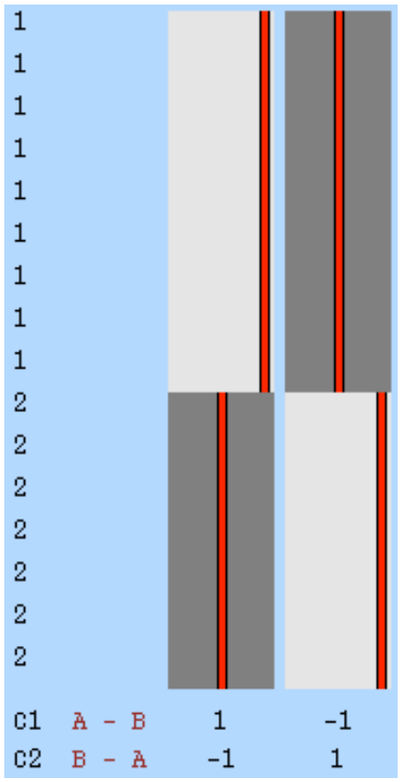

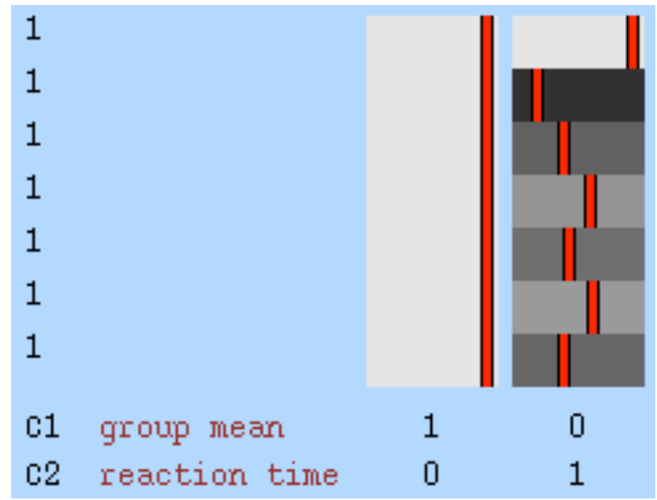

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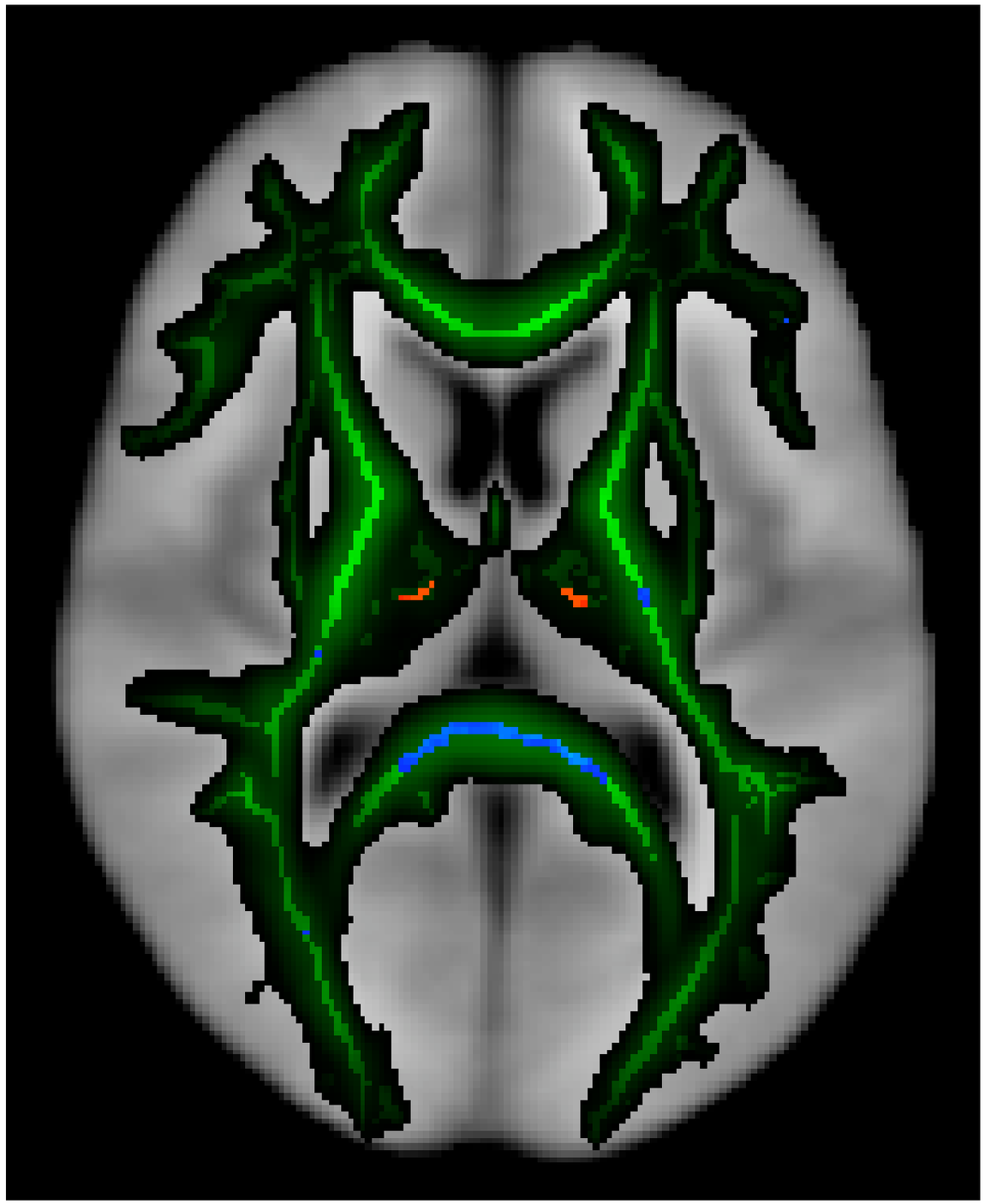
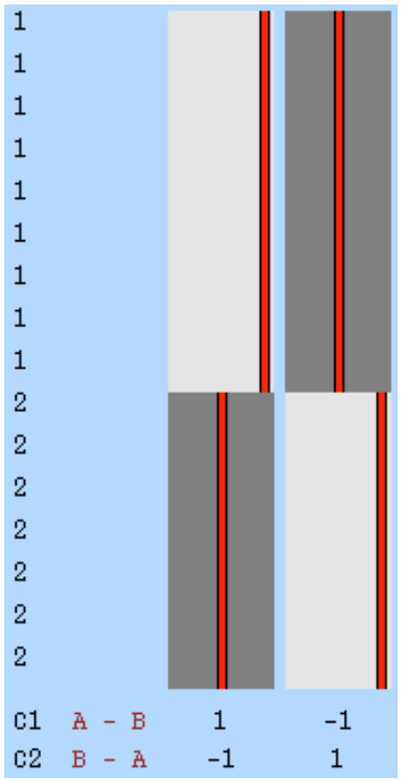
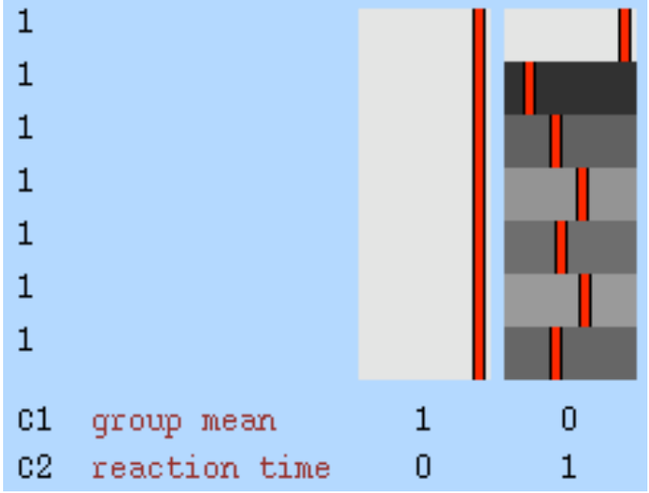
6. Threshold, (e.g., permutation testing, including multiple comparison correction)



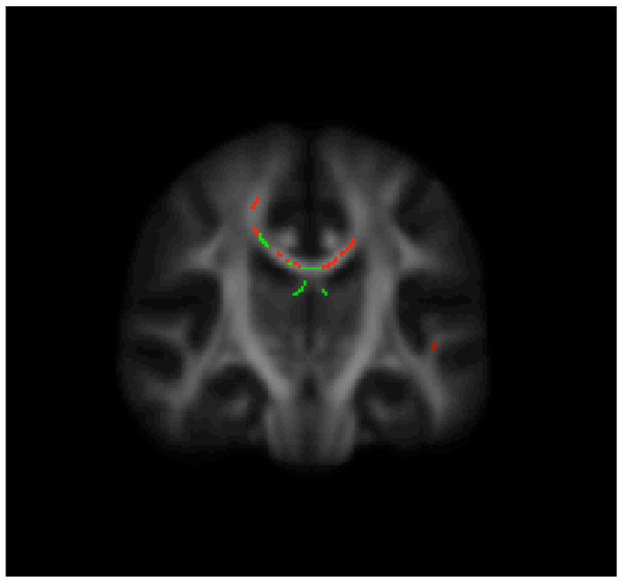


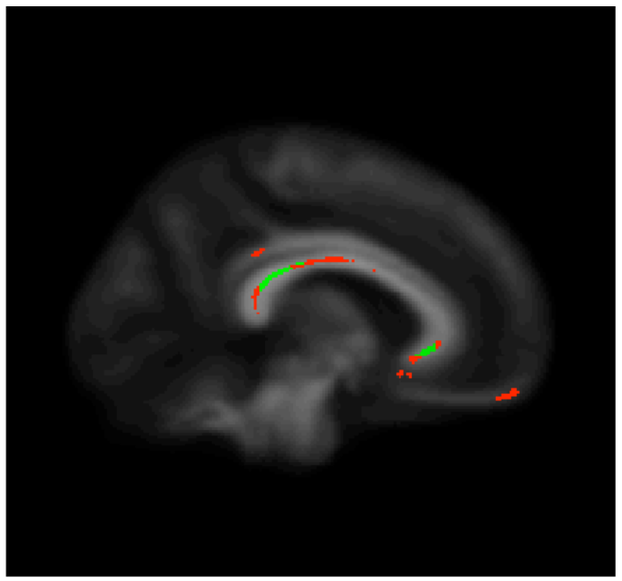


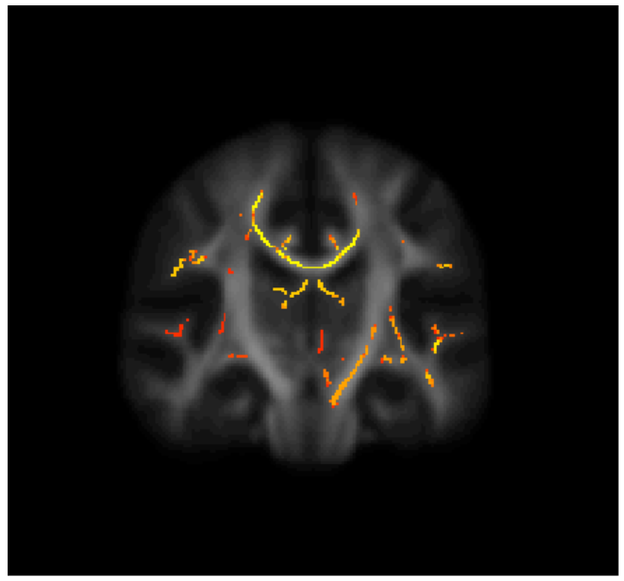
TFCE for TBS

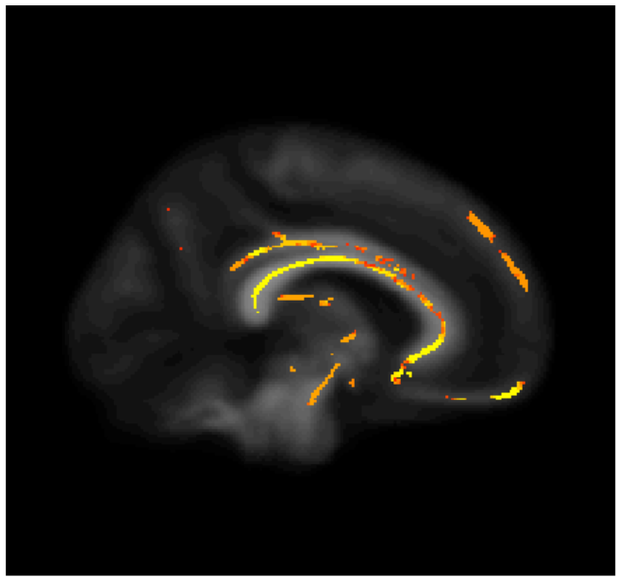
controls > schizophrenics

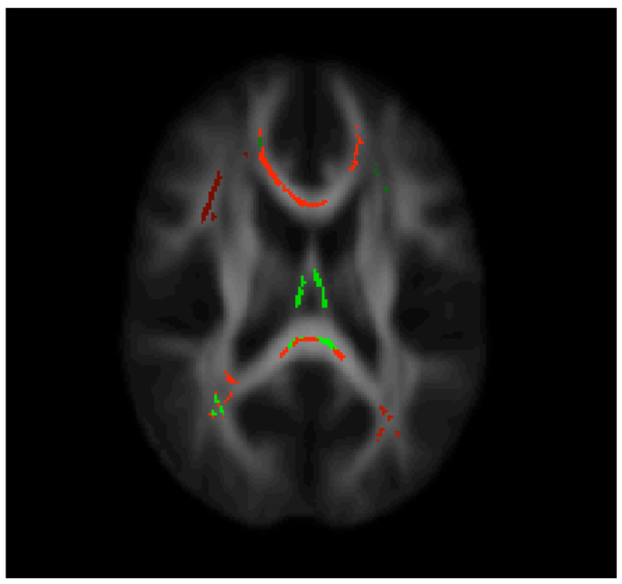
p<0.05 corrected for multiple comparisons across space, using randomise



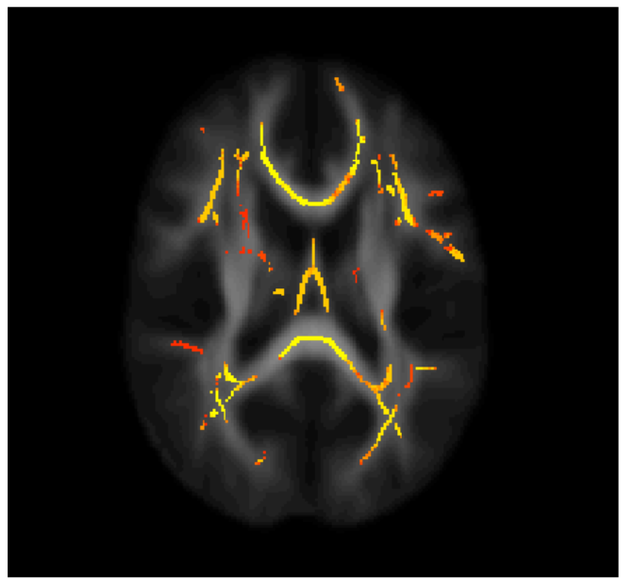








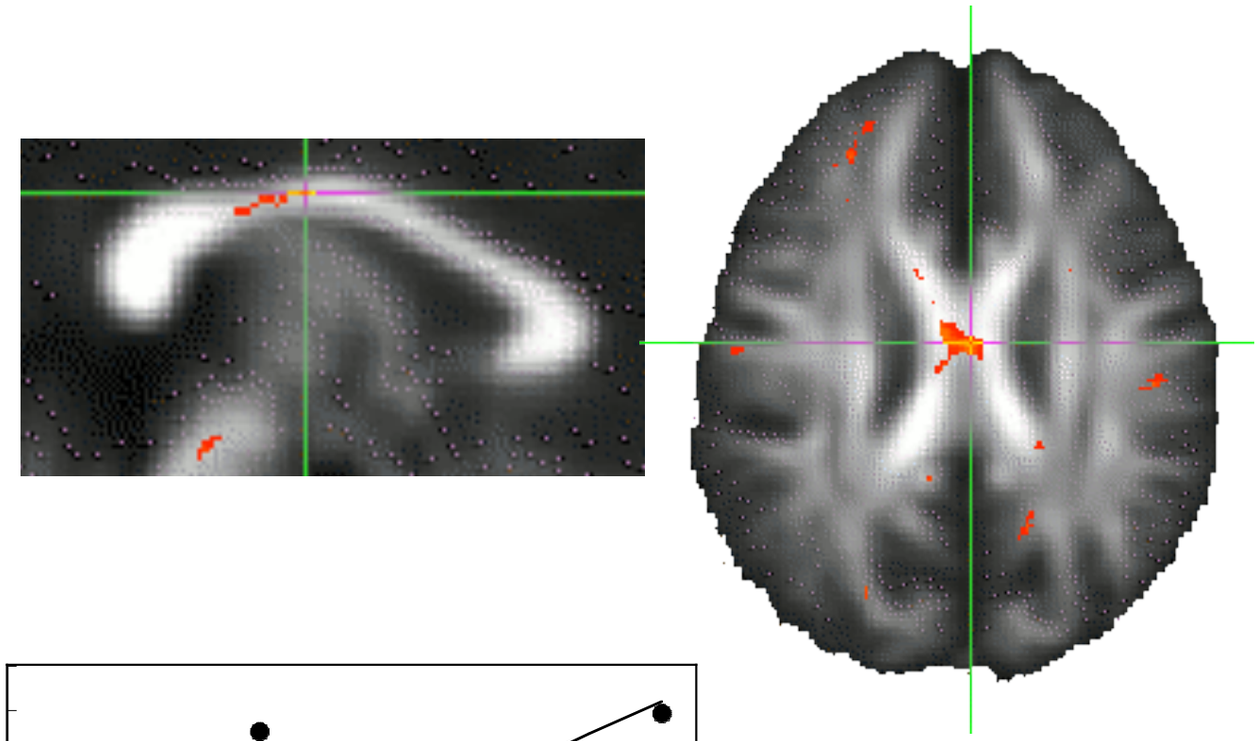
cluster-based:
cluster-forming
threshold =
2 or 3

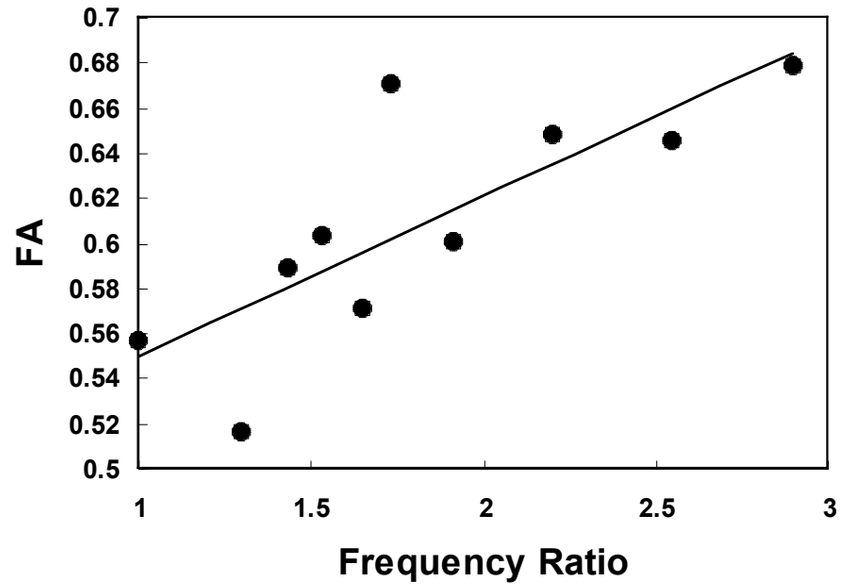


TFCE

Differences in healthy controls

Normal variation in bimanual co-ordination skill



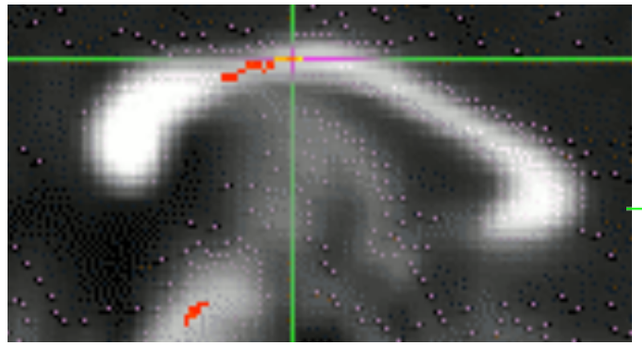


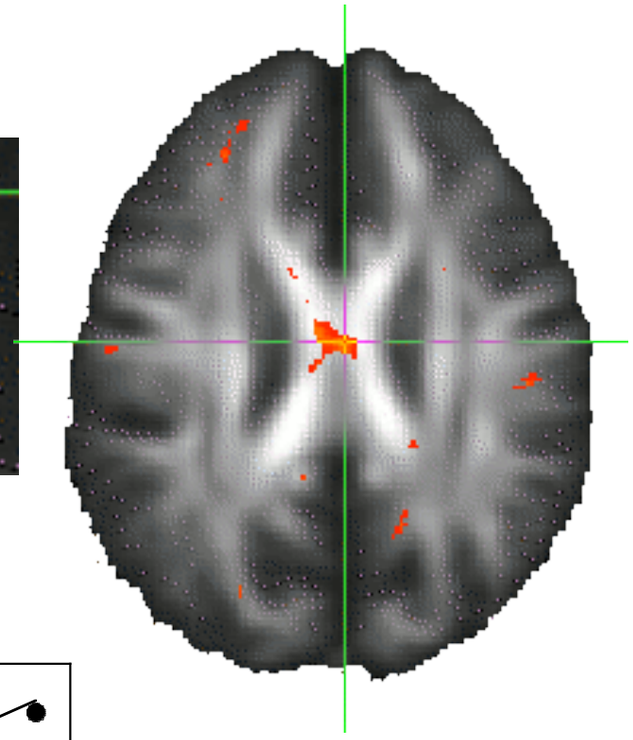
Johansen-Berg et al, OHBM, 2006

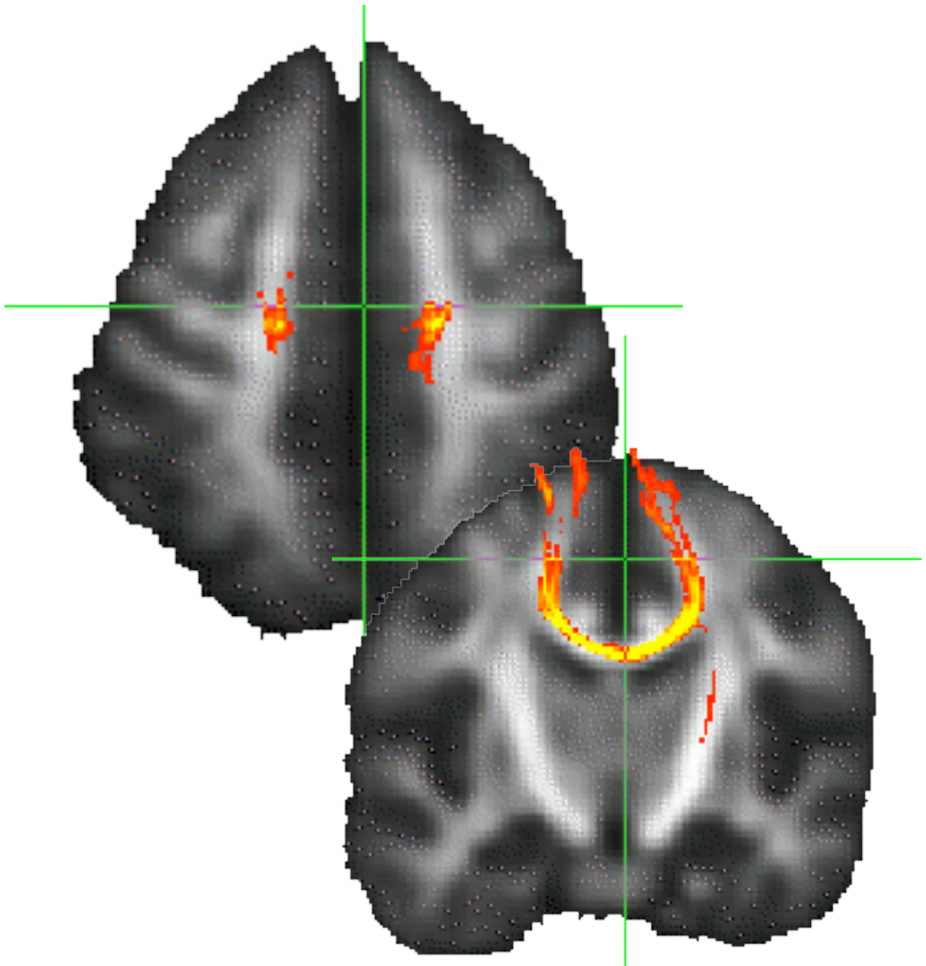
- Inter-individual variation in FA along a specific motor pathway is related to variation in motor skill
- Experience-dependent structural changes?

Differences in healthy controls

Normal variation in bimanual co-ordination skill







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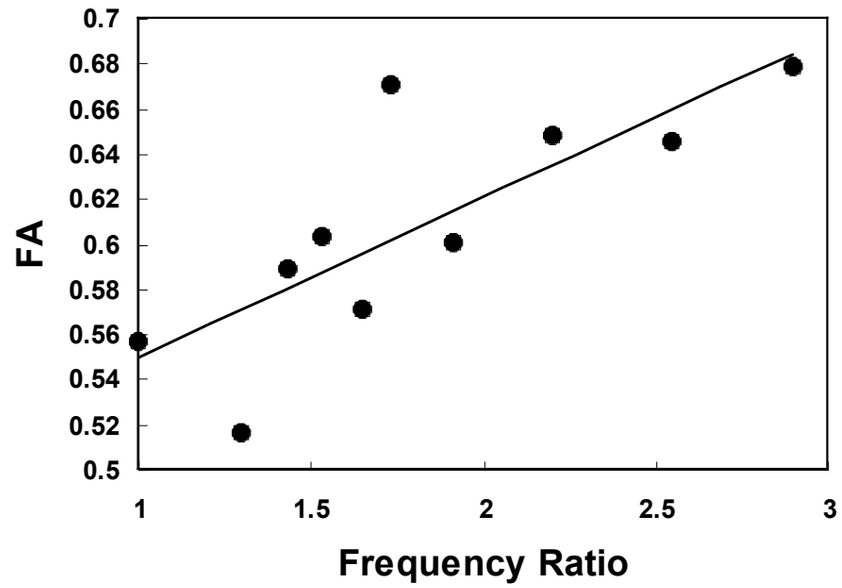
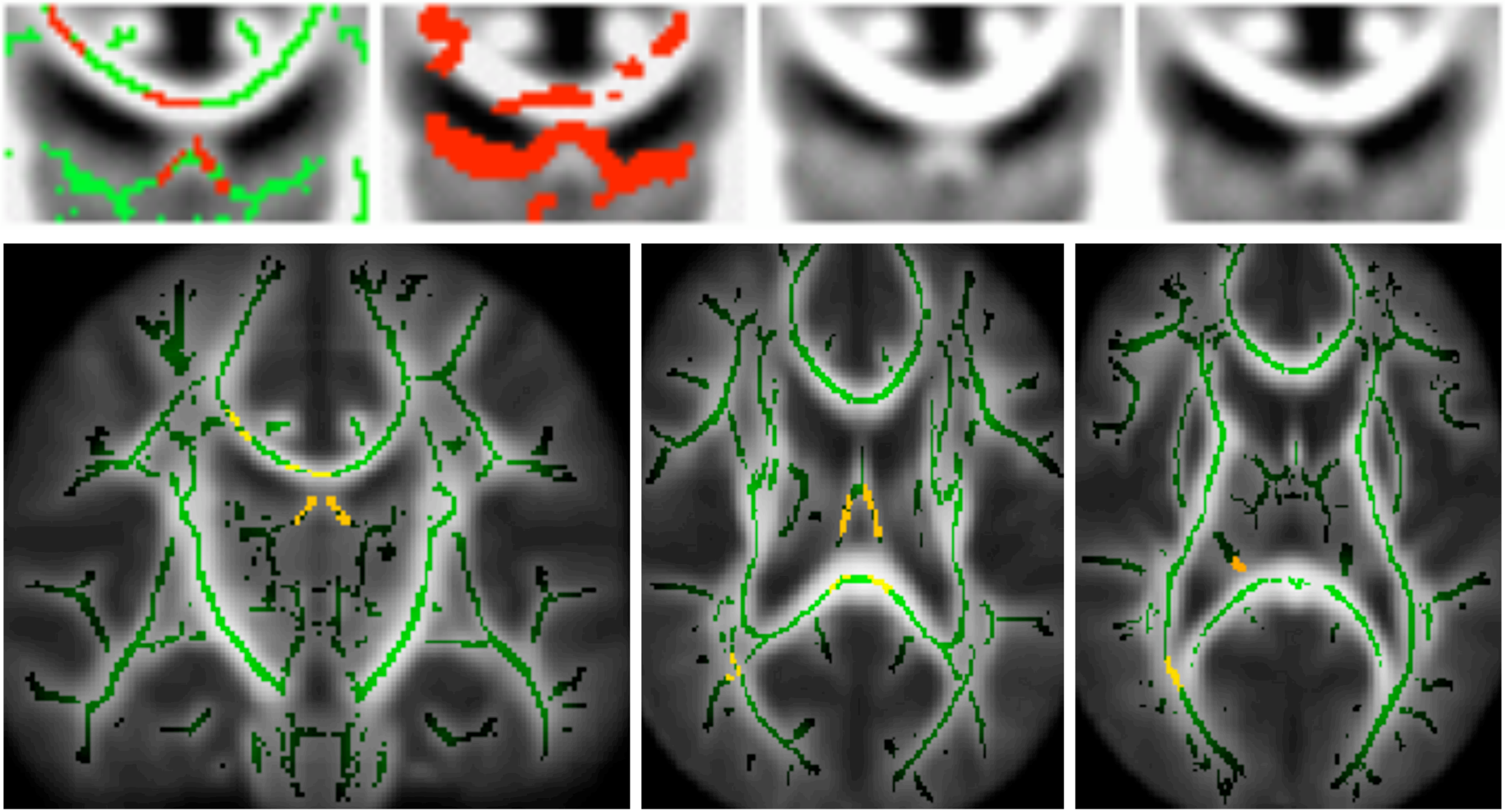


- Inter-individual variation in FA along a specific motor pathway is related to variation in motor skill
- Experience-dependent structural changes?

Schizophrenia (Mackay)

TBSS & VBM show reduced FA in corpus callosum & fornix
VBM shows spurious result in thalamus due to increased ventricles in schiz.

TBSS | VBM | mean FA (controls) | mean FA (schiz.)

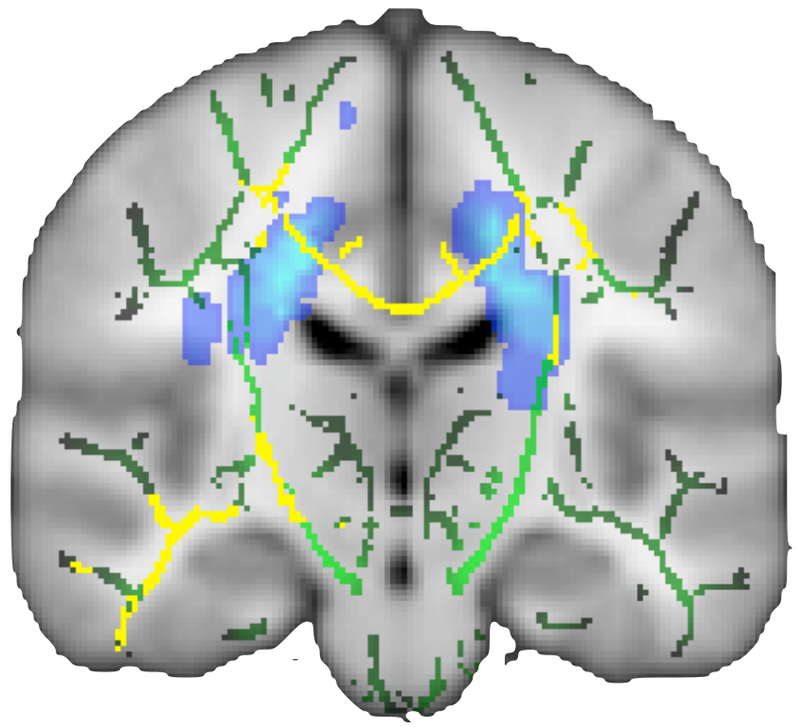


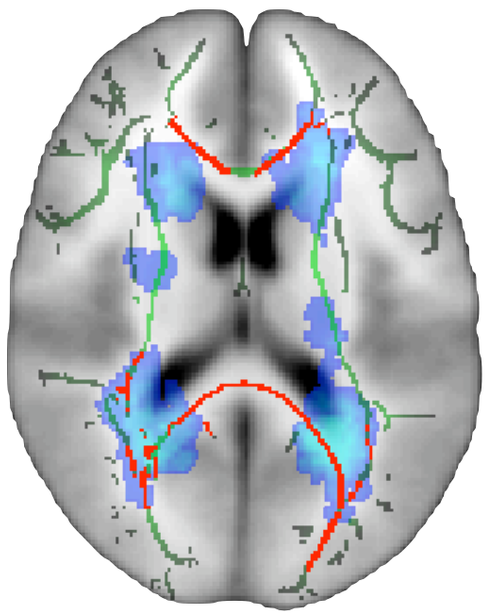
Multiple Sclerosis (Cader, Johansen-Berg & Matthews)

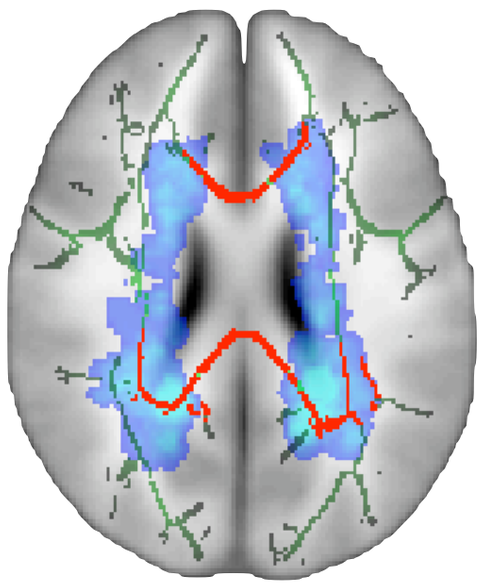
- 15 MS patients

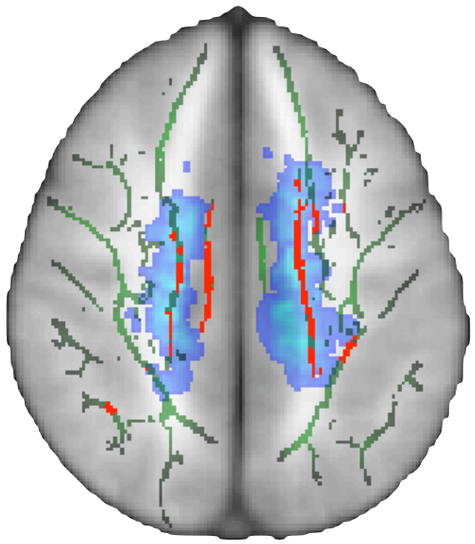
- Yellow = -ve corr. FA vs EDSS

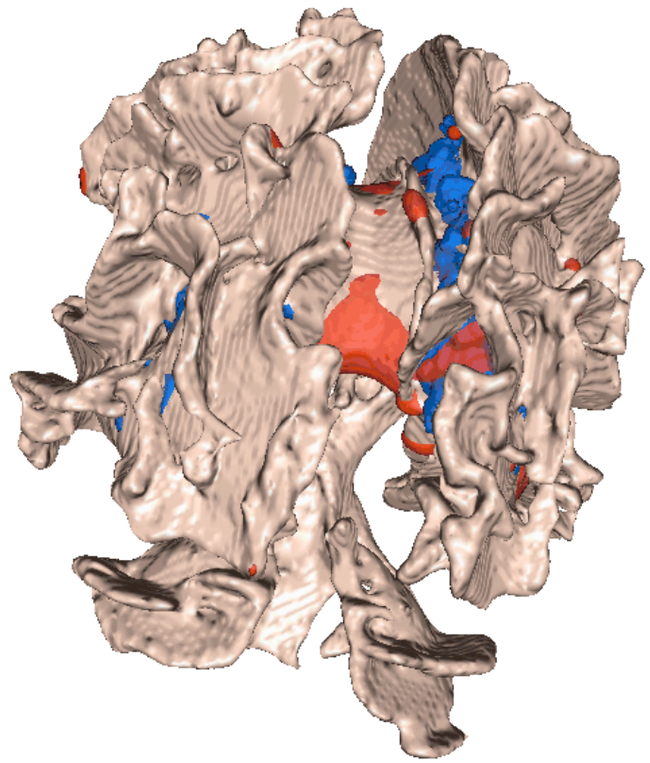
- Blue = group lesion probability (50%)
- Red = -ve corr. FA vs lesion volume
  Note reduced FA away from lesions











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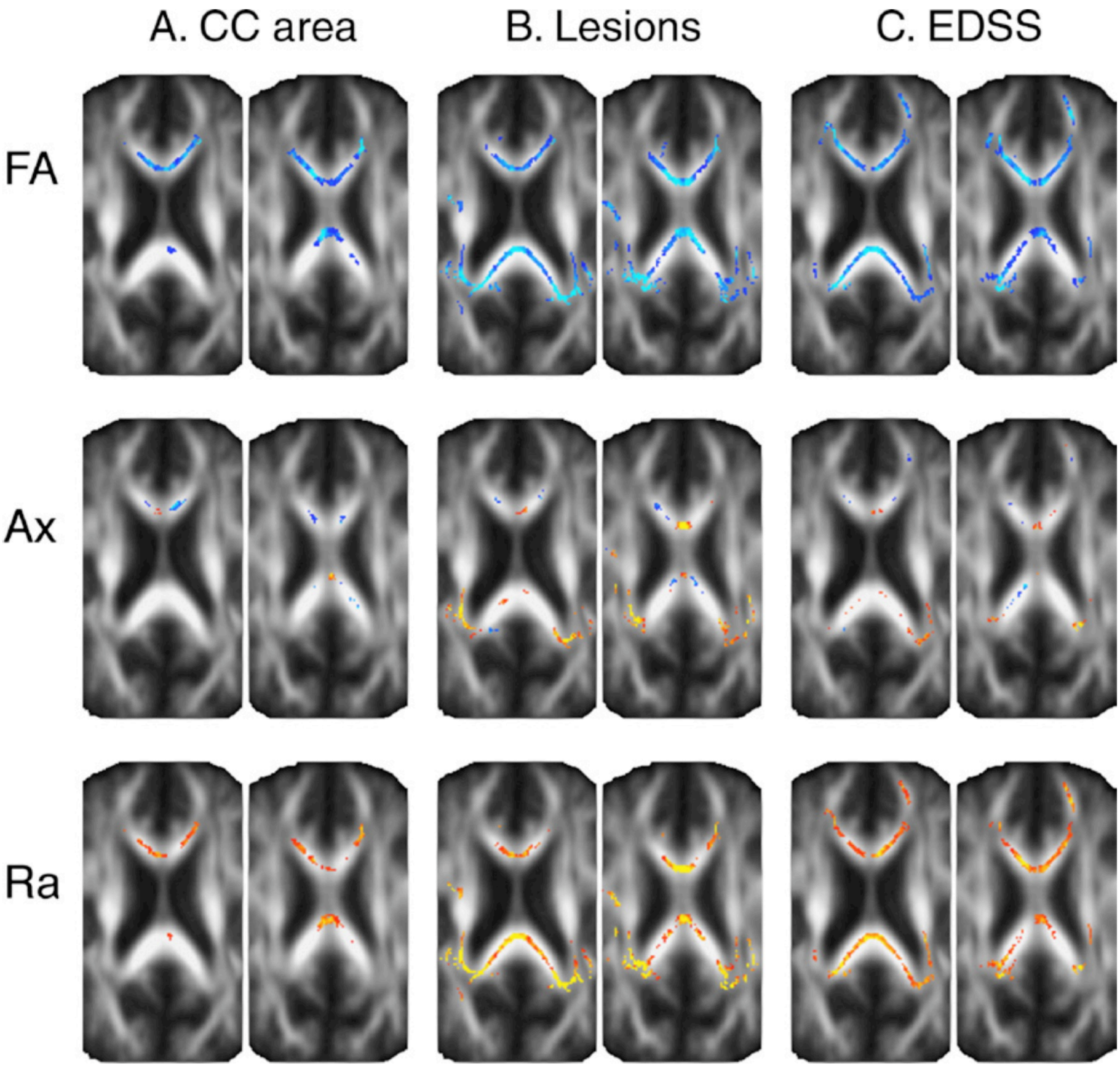
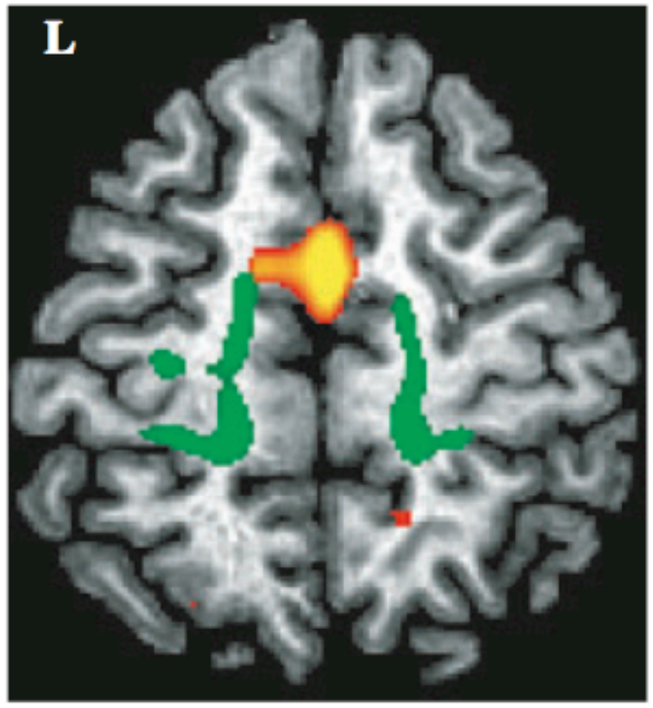
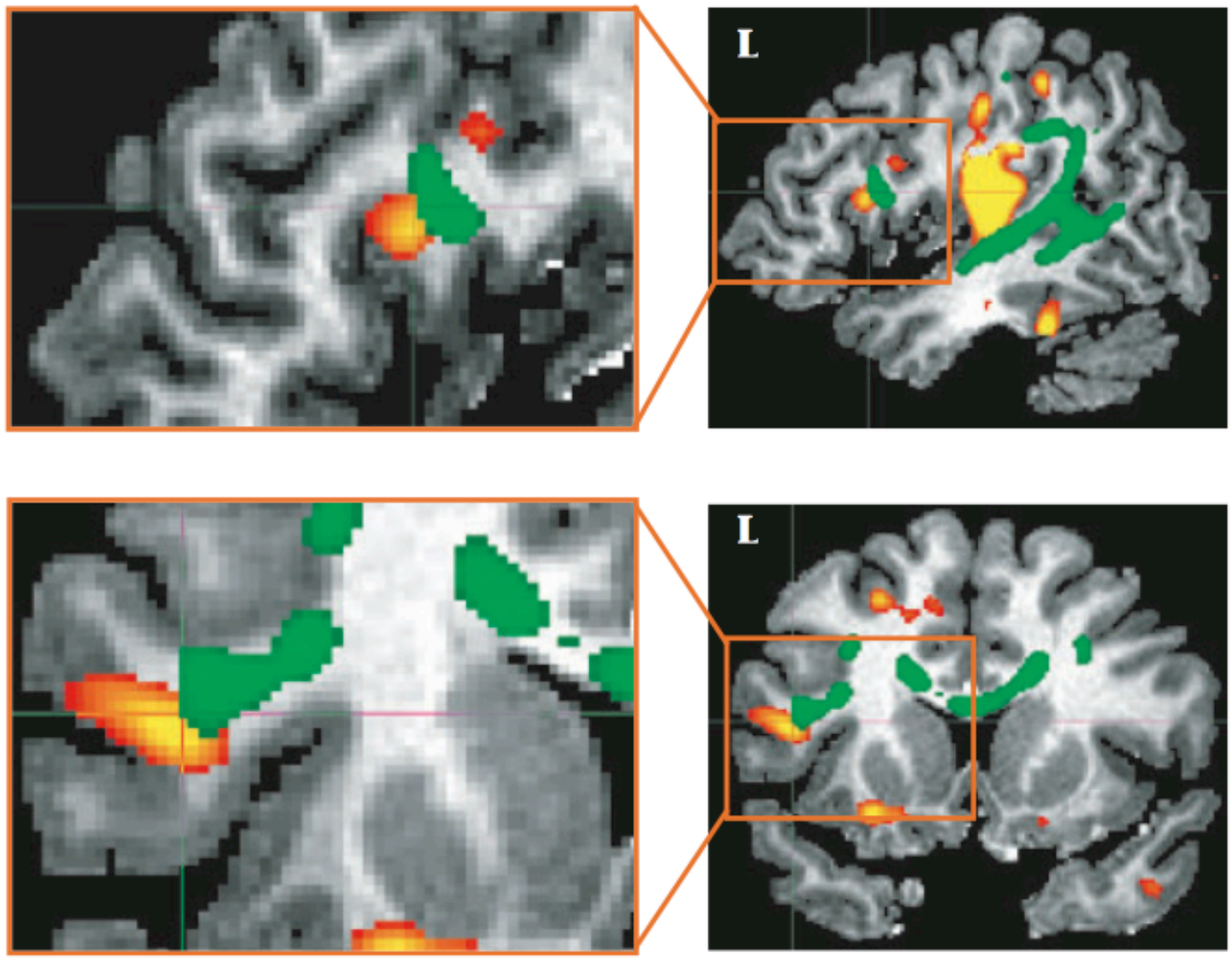


TBSS & FSL-VBM in adolescent-onset schizophrenia Douaud & James, Brain 2007



FA reduction

GM reduction

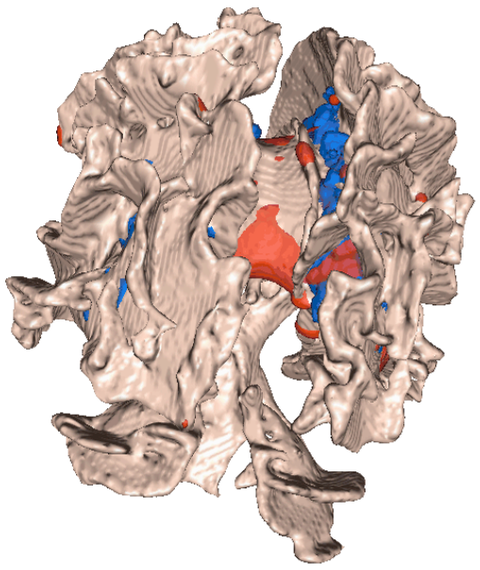


TBSS - Conclusions

- Attempting to solve correspondence/smoothing problems
- Less ambiguity of interpretation / spurious results than VBM
- Easier to test whole brain than ROI / tractography

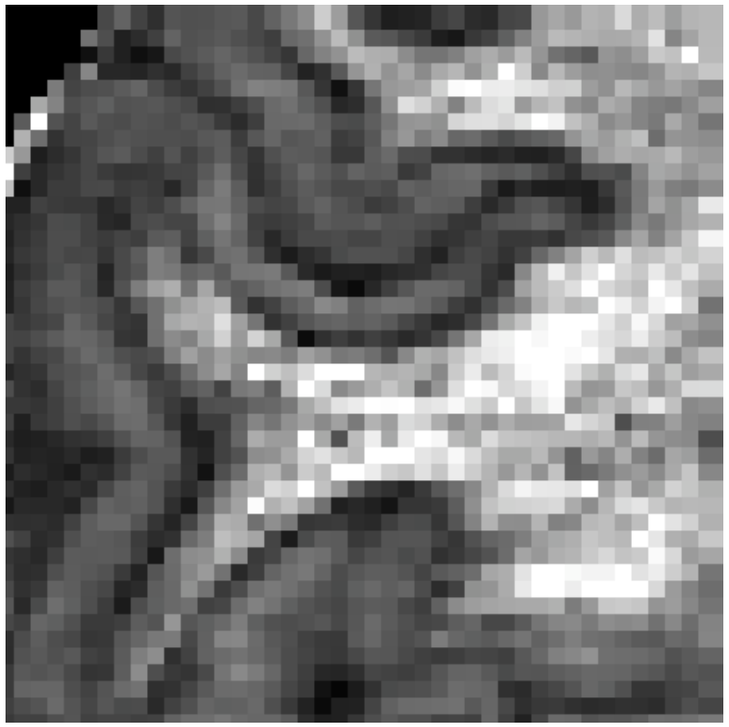
- Limitations & Dangers
  - Interpretation of partial volume tracts still an issue
  - Crossing tracts?

- Future work
  - Use full tensor (for registration and test statistic)
  - Use other test statistics (MD, PDD, width)
  - Multivariate stats (across voxels and/or different diffusion measures) & discriminant (ICA, SVM)



At “normal” resolutions, tracts appear thinner than they really are

primarily because of the interference between orthogonal anisotropy in GM and WM



original 0.7mm data -> FA

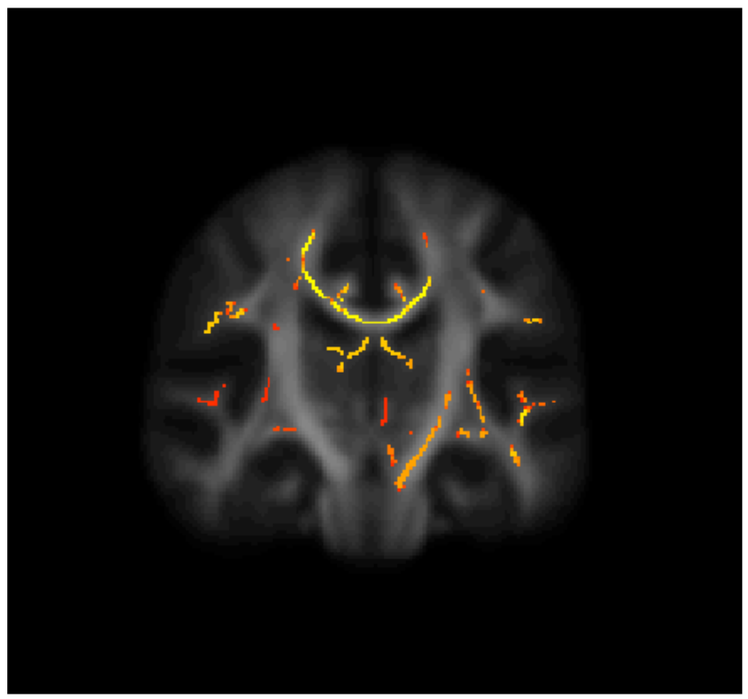
data smoothed to match
2mm data -> FA

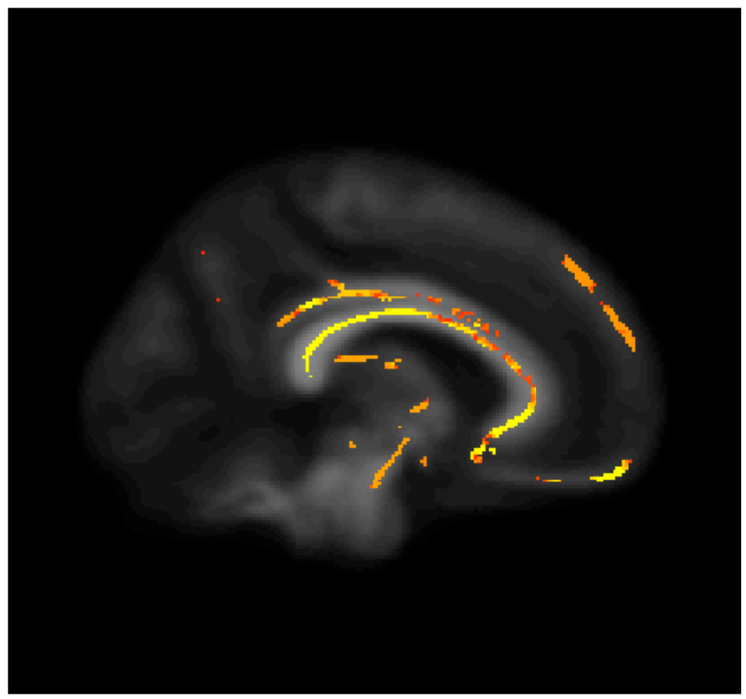
data smoothed to match
3.5mm data -> FA

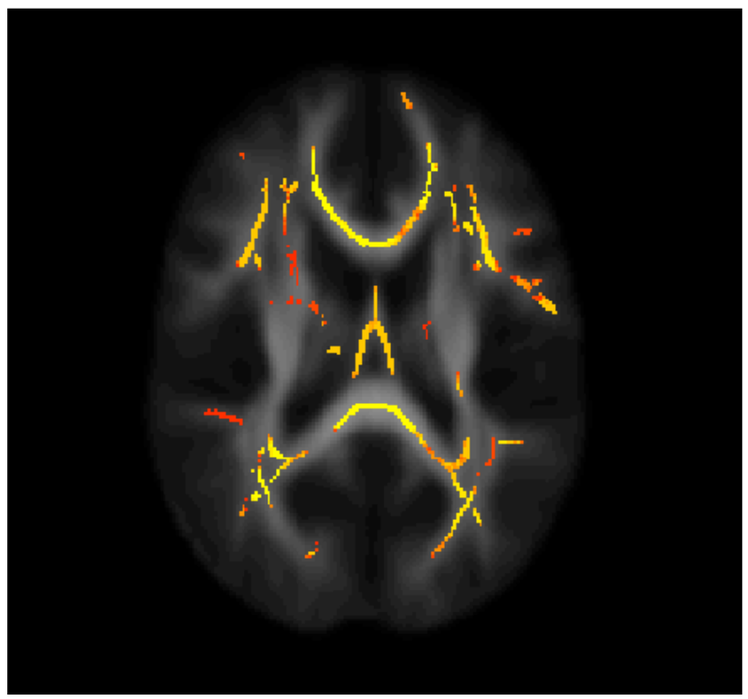
high-resolution ex-vivo diffusion data:
McNab & Miller (FMRIB)

computation resources:
Jones, Stathakis & Wise (CUBRIC cluster)

Disambiguating PVE changes from FA changes







- Even with the TBSS approach, if a tract is of similar size to voxels (or smaller), there will be partial-volume effects at the tract centre
- Hence: is an apparent change in FA caused by a change in partial voluming across subjects, or a change in true FA?
- Hard to disambiguate

Disambiguating PVE changes from FA changes

F: original high-resolution “ground truth” MD image

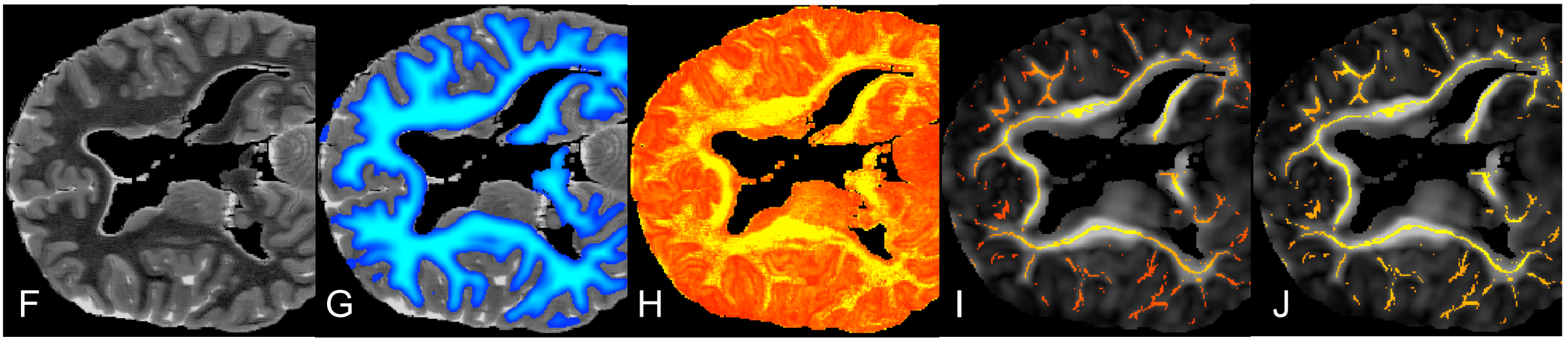
G: WM PVE as it would appear in normal-res data
(high-res MD -> FAST segmentation -> high-res WM PVE -> normal-res WM PVE)

H: original high-resolution “ground truth” FA

I: normal-res FA
(downsample original data -> form FA -> TBSS skeletonise)

J: “corrected” normal-res FA on skeleton
(feed apparent normal-res FA and normal-res WM PVE into correction model)

Quadratic model of trueFA = f(apparentFA,WM-PVE) works well



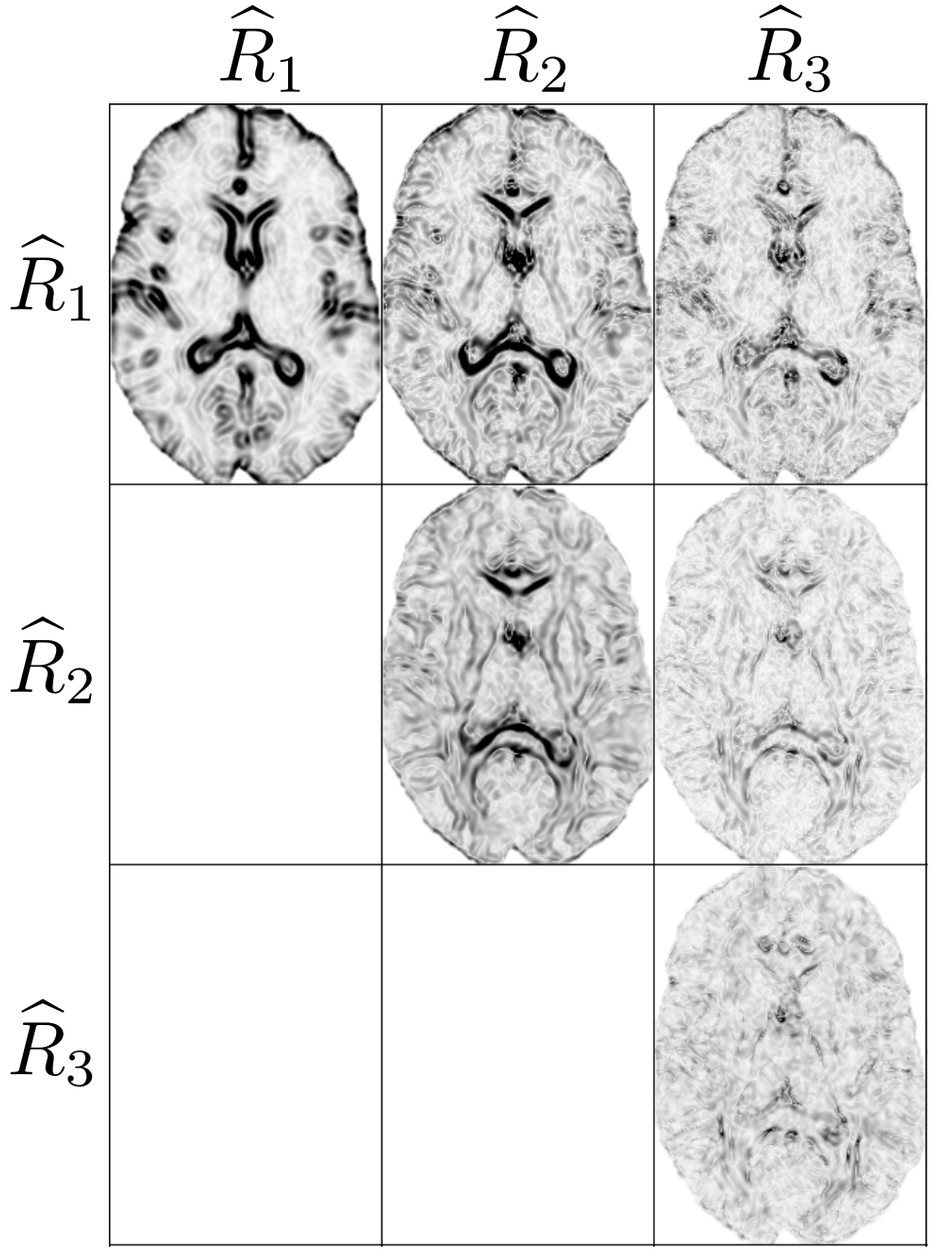
high-resolution ex-vivo diffusion data: McNab & Miller (FMRIB) *computation resources: Jones, Stathakis & Wise (CUBRIC cluster)*

Disambiguating PVE changes from FA changes

So....model trueFA = f(apparentFA,WM-PVE) worked well....**but** in “normal” data we don’t have access to such a nice tissue-type segmentation from the same diffusion acquisition.....

Hence: the “tensor-covariance” is useful [Kindlmann, IEEE-TMI 2007]. This describes how the tensor at a voxel covaries with neighbouring tensors, and hence contains useful information about effects of PVE, tract-thinning, etc.

So: use model trueFA = f(apparentFA, tensor-covariance)



Disambiguating PVE changes from FA changes

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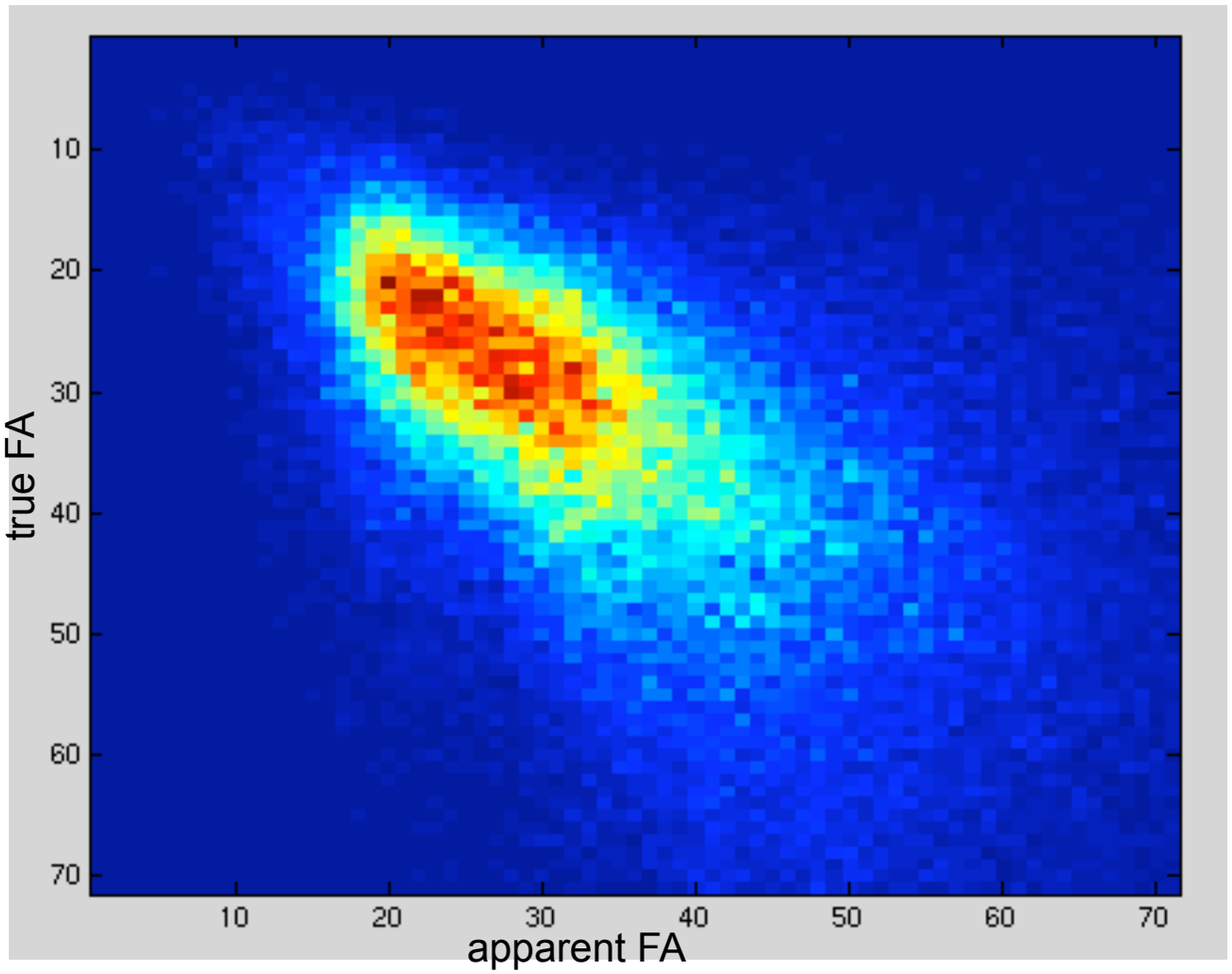

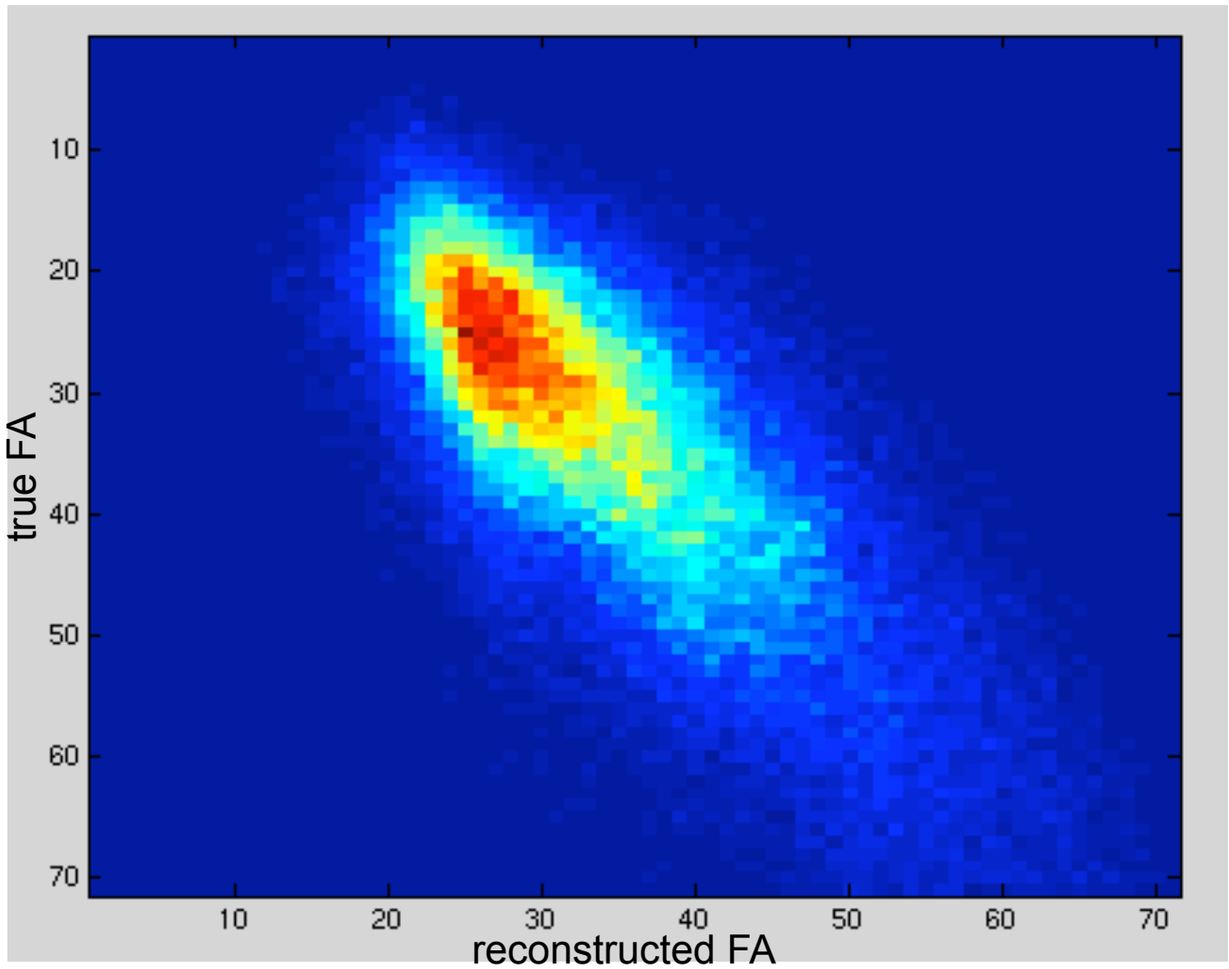

high-resolution ex-vivo diffusion data: McNab & Miller (FMRIB)

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