

# Multi-modality processing with Advanced Normalization Tools (ANTs)

Brian Avants, PICSL and the ANTs Development Team

May X 2015

- 1 Background and basics
- 2 ANTs Software Summary
- 3 ANTs registration
- 4 Template based studies
- 5 Population statistics
- 6 Multiple modality processing

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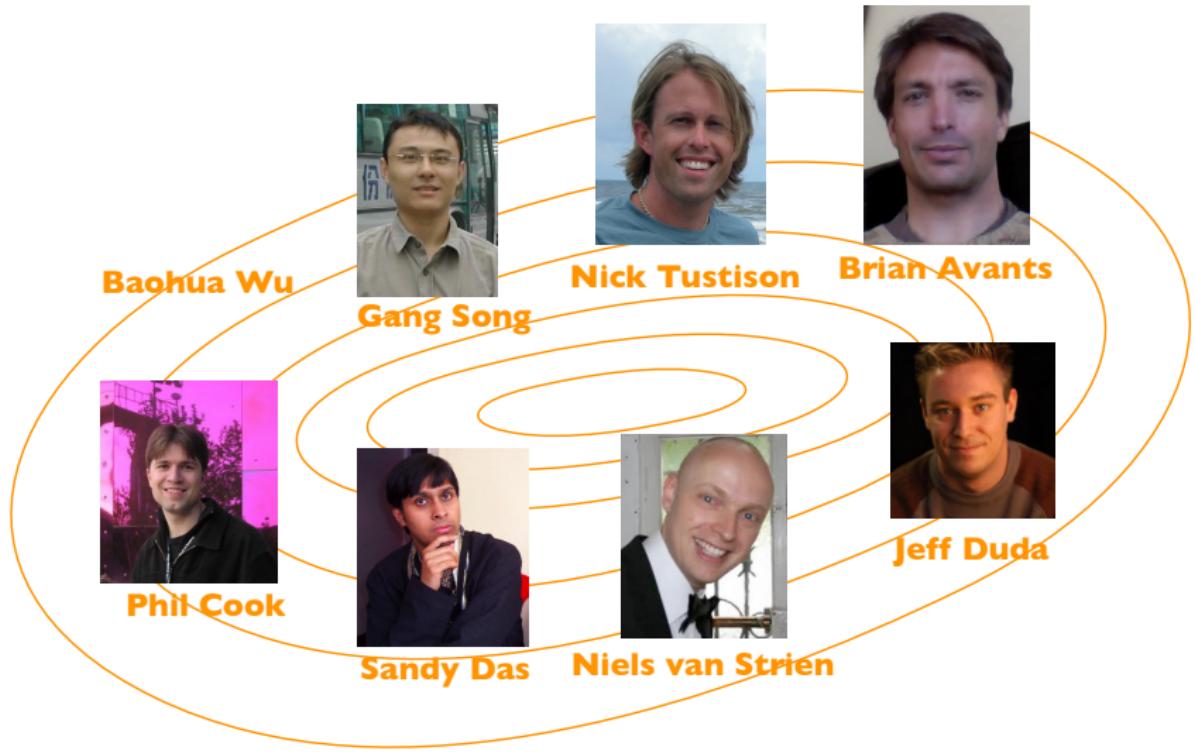
## Simple hints for ...



Surfboard riders using their arms for balancing as they rocket along on the forward slope of a racing wave

WHERE the sea throws itself shore- material and type of construction. For wave

# People



# History: Theory



# History: Implementation

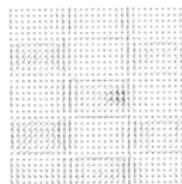


Fig. 550. Skull of chimpanzee.



Fig. 551. Skull of baboon.

## DETERMINING OPTICAL FLOW

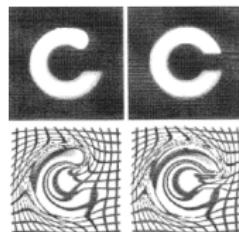


Thompson 1917

TRANSACTIONS ON IMAGE PROCESSING, VOL. 5, NO. 10, 1

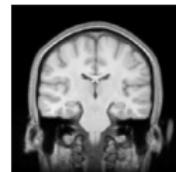


Gee 1994



Miller 1996

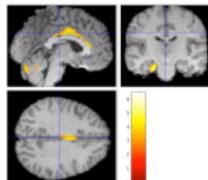
Horn 1980



(a) Coronal slice, elastic registration.

Guimond 1999

Bajcsy 1988



Ashburner 2000

# Download ANTs binaries

- Go to: <http://stnava.github.io/ANTs/>

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- Select the right version for your platform.

# Download ANTsR binaries

- Go to: <http://stnava.github.io/ANTsR/>

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- Go to: <http://stnava.github.io/ANTsR/>
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- Select the latest release for your platform then:

# Download ANTsR binaries

- Go to: <http://stnava.github.io/ANTsR/>
- You will see links for documentation, code, binaries.
- Select the latest release for your platform then:
- R CMD INSTALL ANTsR\*tar.gz

# Install ANTs from source: Requires git, cmake, C++

open a terminal window and then type

```
$>$ git clone http://github.com/stnava/ANTs.git
```

```
$>$ mkdir bin
```

```
$>$ cd bin/
```

```
$>$ ccmake ../ANTS/
```

# Install ANTs from source: Requires git/svn, cmake, C++

then, in cmake, type **c** and then **g** then exit back to the terminal. then:

```
$>$ make -j 4
```

and wait a while.



# Overview: Program + brief description

---

Tool	Description
ANTS	Interface to variety of registration algorithms
antsRegistration	ITKv4 update to ANTS
Atropos	Multivariate probabilistic EM segmentation
N4BiasFieldCorr	Novel inhomogeneity field correction method
ImageMath	Basic operations on images.
buildtemplateparallel	Optimal templates in the diffeomorphic space.
WarpImageMultiTrans	Concatenates ANTS/ITK transforms
antsApplyTransforms	Concatenates ANTS/ITK transforms
KellyKapowski	Cortical thickness directly from imaging
sccan	Multivariate dimensionality reduction
antsMotionCorr	Motion correction and more for space-time images

---

# Overview: Program + brief highlights

Tool	Highlights
ANTS	Frequent winner in registration competitions.
antsRegistration	Takes full advantage of multicore processing.
Atropos	Can integrate information from multiple modalities.
N4BiasFieldCorr	New standard in inhomogeneity correction.
ImageMath	Works on 2D, 3D, 4D images.
buildtemplateparallel	New multimodality implementation.
WarpImageMultiTrans	Can string together a series of N transforms.
antsApplyTransforms	Can string together a series of N transforms.
KellyKapowski	Multi-platform volumetric alternative to Freesurfer
sccan	DimRed methods improve detection power in imaging
antsMotionCorr	Rigid, affine, deformable motion correction.

# Overview: Program + primary reference

Tool	Primary Reference
ANTS	A reproducible evaluation of ANTs similarity metric
antsRegistration	A unified registration framework for ITK.
Atropos	An open source multivariate framework for n-tissue segmentation.
N4BiasFieldCorr	N4ITK: improved N3 bias correction.
ImageMath	—
buildtemplateparallel	The optimal template effect in hippocampus studies
WarpImageMultiTrans	-
antsApplyTransforms	-
KellyKapowski	Registration based cortical thickness measurement.
sccan	Dementia induces correlated reductions in white matter integrity.
antsMotionCorr	The pediatric template of brain perfusion

# ANTs is good for scripting large-scale studies

# App-like framework

- ANTs likes short bash scripts

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- Longer scripts should use R, ANTsR or perl

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- ANTs likes short bash scripts
- Longer scripts should use R, ANTsR or perl
- `#! /usr/bin/Rscript`

# The Basic Toolset

- Registration: Data is in Examples/Data

```
ANTS 2 -m CC[r16slice.nii.gz,r64slice.nii.gz,1,4]
-t SyN[0.25] -r Gauss[3,0] -o TEST -i 50x40x30
```

ants-essential tools: a mapping, a segmentation, a template and then label-guided and multivariate versions of these.

# The Basic Toolset

- Registration: Data is in Examples/Data

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ANTS 2 -m CC[r16slice.nii.gz,r64slice.nii.gz,1,4]
-t SyN[0.25] -r Gauss[3,0] -o TEST -i 50x40x30
```

- Segmentation

```
Atropos -d 2 -a r16slice.nii.gz -x r16mask.nii.gz
-m [0.1,1x1] -c [10,0] -i kmeans[3]
-o [Output.nii.gz,Output\_prob\_\%02d.nii.gz]
```

ants-essential tools: a mapping, a segmentation, a template and then label-guided and multivariate versions of these.

# The Basic Toolset

- Registration: Data is in Examples/Data

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ANTS 2 -m CC[r16slice.nii.gz,r64slice.nii.gz,1,4]
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```

- Segmentation

```
Atropos -d 2 -a r16slice.nii.gz -x r16mask.nii.gz
-m [0.1,1x1] -c [10,0] -i kmeans[3]
-o [Output.nii.gz,Output\_prob\_\%02d.nii.gz]
```

- Template building

```
buildtemplateparallel.sh -d 3 -m 30x50x20
-t GR -s CC -c 1 -o OutPrefix *ImageName*T1x.nii.gz
```

ants-essential tools: a mapping, a segmentation, a template and then label-guided and multivariate versions of these.

# Basic applications

- Quantify changes in cortical thickness in an individual.

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- Asymmetry study of neuroanatomy.

# Basic applications

- Quantify changes in cortical thickness in an individual.
- Perform a template-based study of thickness, gray matter probability, FA, rs connectivity ...
- Identify multivariate relationships between modalities and predictors.
- Single-subject BOLD fmri study of resting state connectivity.
- Asymmetry study of neuroanatomy.
- In general, optimal dimensionality reduction to increase detection power.

# Segmenting anatomy from an image

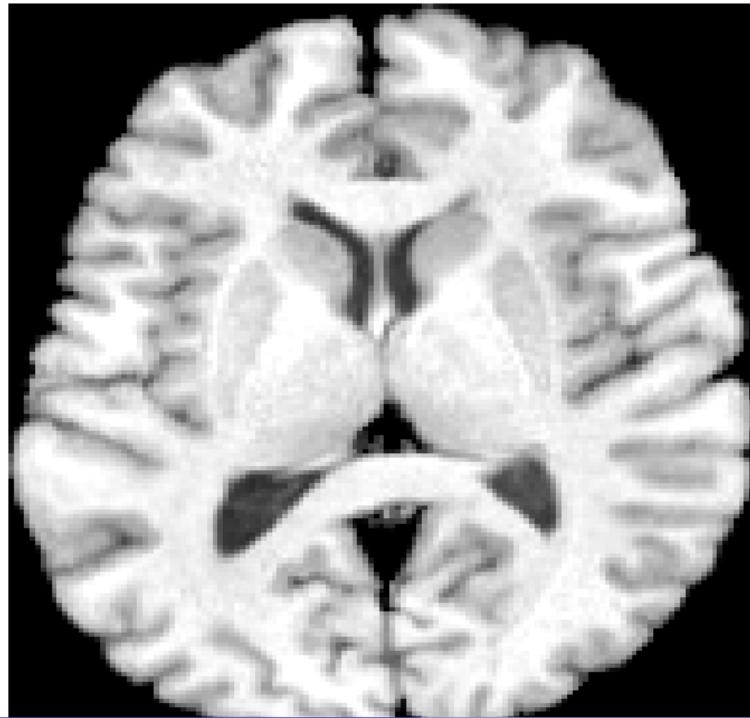
```
ThresholdImage $dim $img ${out}mk.nii.gz 0.2 1.e9
ImageMath $dim ${out}mk.nii.gz ME ${out}mk.nii.gz 2
ImageMath $dim ${out}mk.nii.gz MD ${out}mk.nii.gz 2
Atropos -d $dim -a $img -x ${out}mk.nii.gz -m [0.05,1x1] \
-c [10,0] -i kmeans[3] \
-o [${out}.nii.gz,${out}prob%02d.nii.gz]
```

# Segmenting anatomy from an image: *ANTsR*

```
fi<-antsImageRead( getANTsRData("r16") )  
fi<-n4BiasFieldCorrection( fi, 4 )  
seg<-kmeansSegmentation( fi, 3 )
```

# Segmenting anatomy from an image: *ANTsR*

```
plot(fi)
```

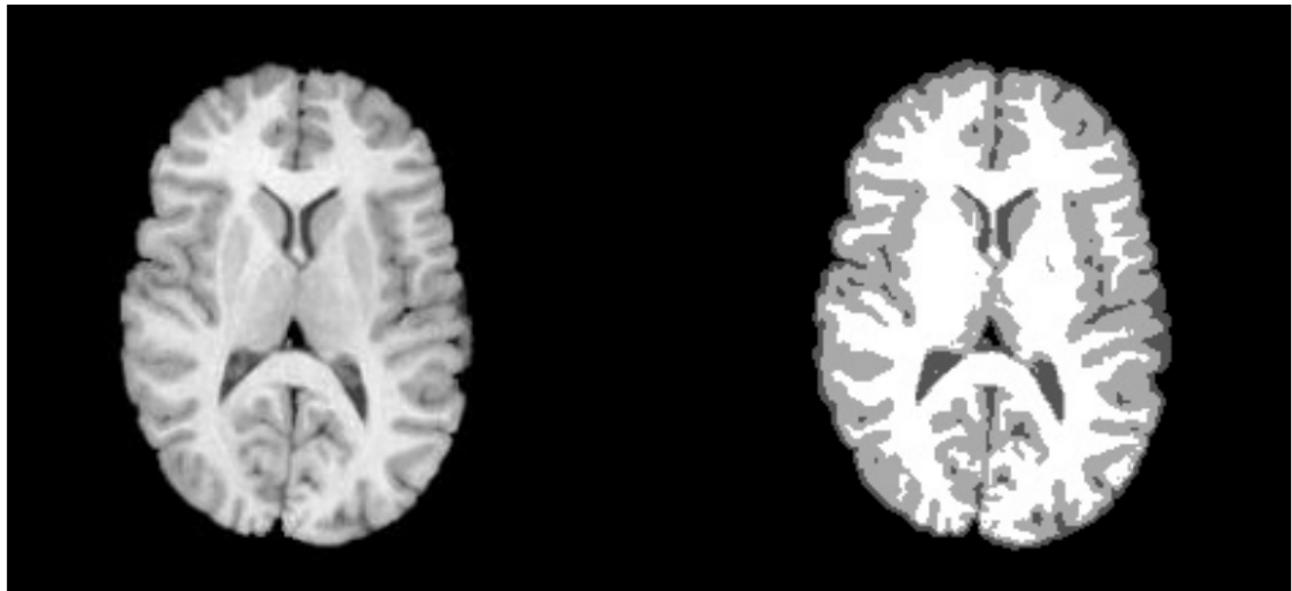


# Segmenting anatomy from an image: *ANTsR*

```
plot(seg$segmentation)
```



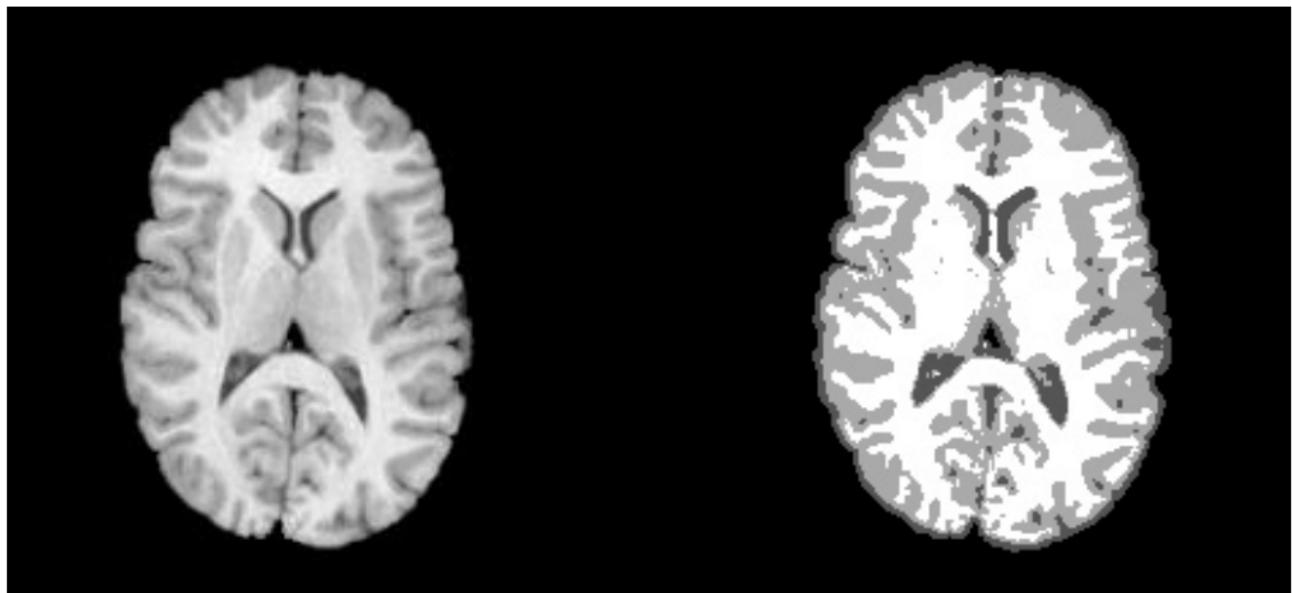
# Segmenting anatomy from an image



# Multivariate anatomical segmentation

```
img <- antsImageRead( getANTsRData("r16") )
mask = getMask(img)
limg = iMath(img, "Laplacian")
gimg = iMath(img, "Grad")
feats <- list( img, limg, gimg )
segs3 <- atropos( a = feats, m = '[0.2,1x1]' ,
                   c = '[2,0]' , i = 'kmeans[3]' , x = mask )
```

# Multivariate anatomical segmentation



# Meaning of segmentation parameters

What happens when i vary each parameter?

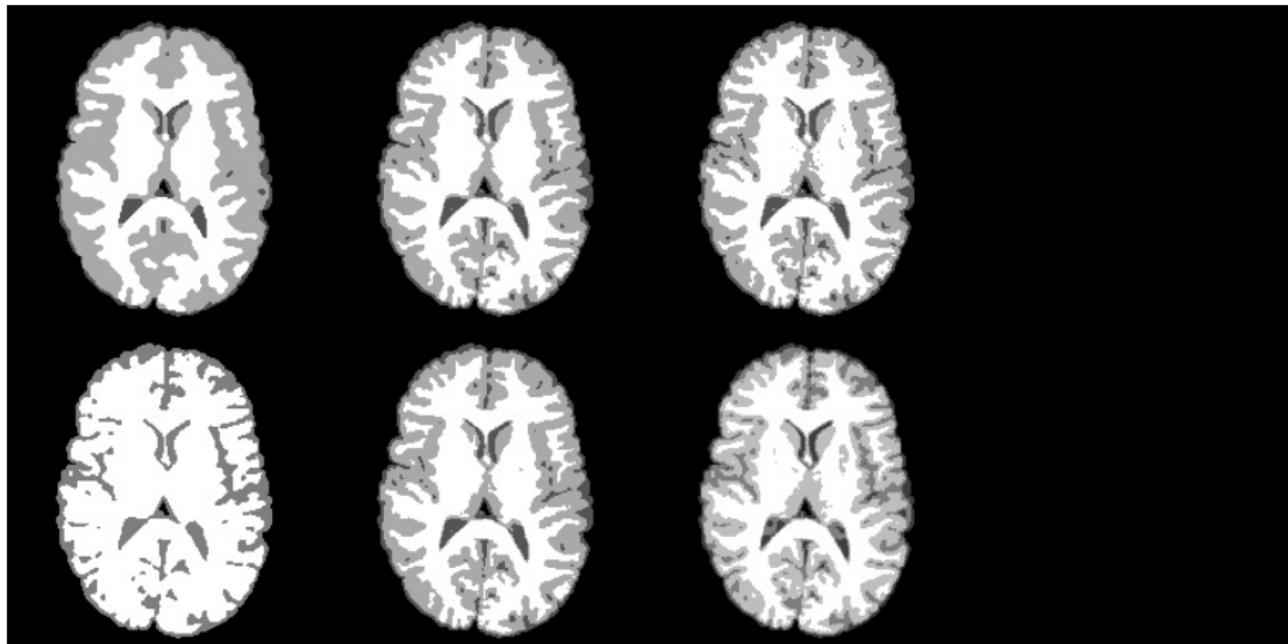
- -m [0.1,1x1] -m [0.2,1x1] -m [0.5,1x1]

# Meaning of segmentation parameters

What happens when i vary each parameter?

- $-m [0.1, 1x1]$     $-m [0.2, 1x1]$     $-m [0.5, 1x1]$
- $-i kmeans[ k ]$  for  $k = 2, 3, 4$

# Meaning of segmentation parameters



Vary MRF param and K in k-means.

# Cortical thickness from imaging data

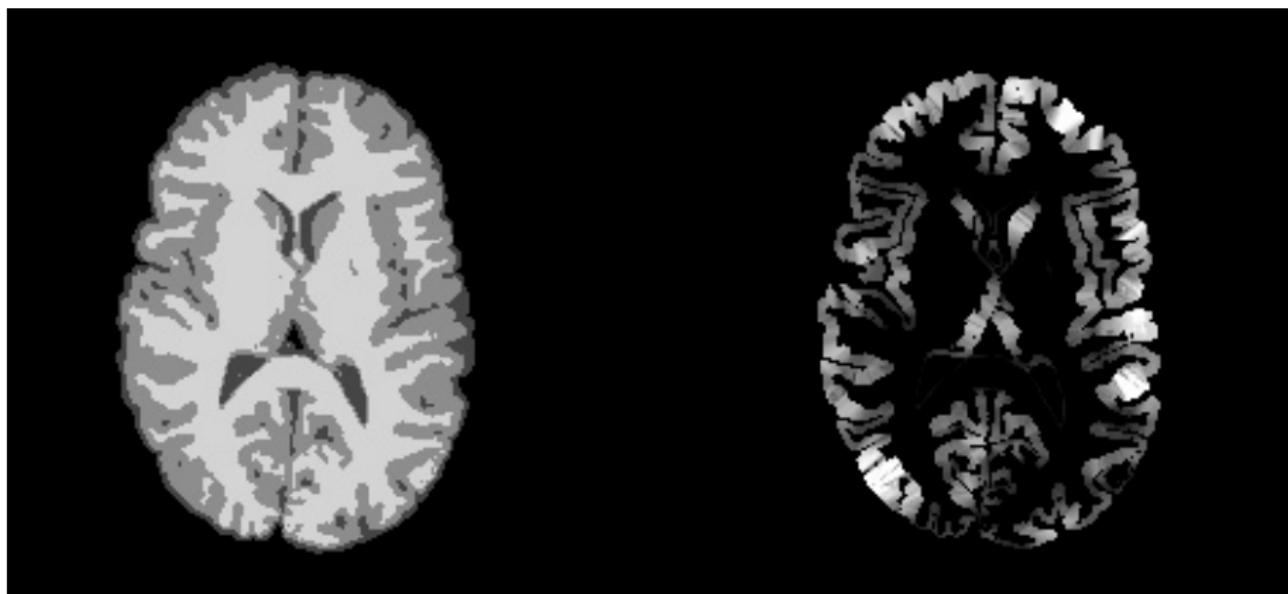
## Command line

```
KellyKapowski -d $dim -s ${out}.nii.gz -g ${out}prob02.nii.gz \
-w ${out}prob03.nii.gz -o ${out}thickness.nii.gz \
-c [30,0] -r 0.5 -m 1.0
```

## In R

```
thk<-kellyKapowski( s=segs$segmentation,
g=segs$probabilityimages[[2]],
w=segs$probabilityimages[[3]],its=45,r=0.5,m=1 )
```

# Cortical thickness from imaging data



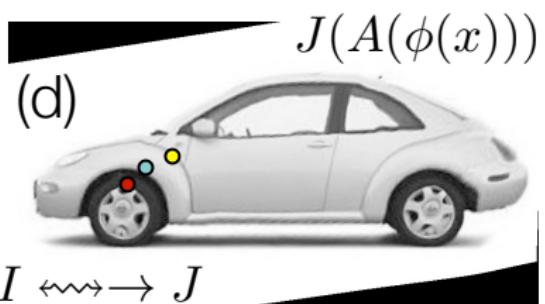
Can vary smoothness, priors on thickness, etc. See help.

# ANTs registration

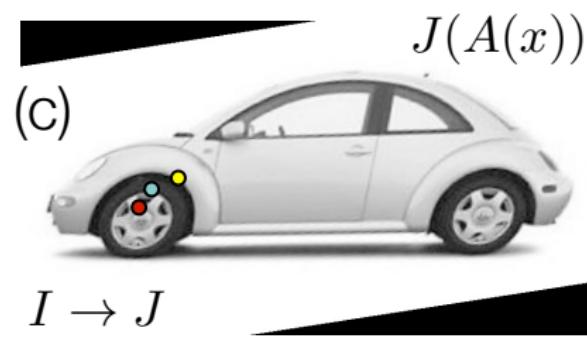
# Template-based transformations



$x$  ●  
 $y$  ○  
 $z$  ○



$I \longleftrightarrow J$



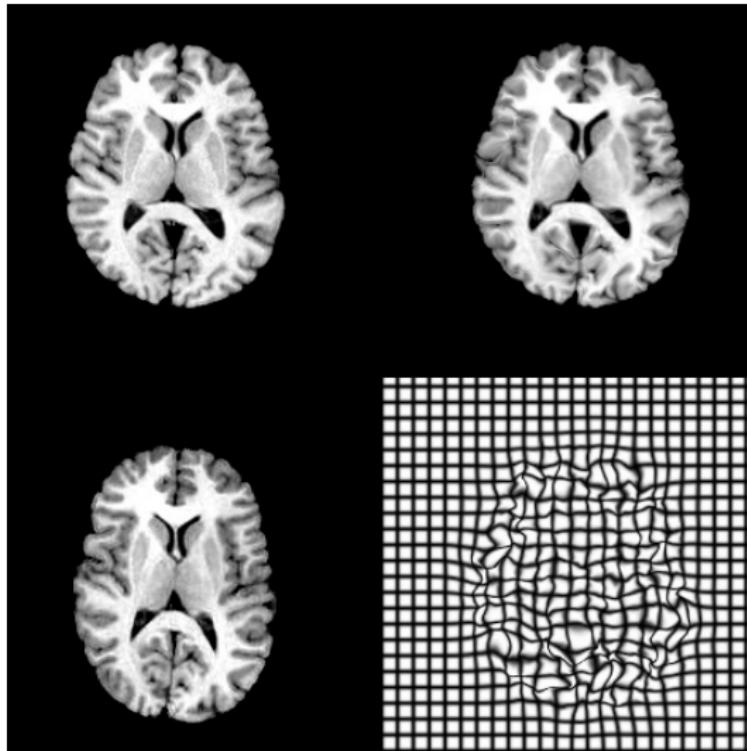
# How did we compute that transformation?

see the web example <http://stnav.a.github.io/cars/>

# Mapping two images

```
antsRegistration -d $dim \
    -r [ $img1, $img2, 1 ] \
    -m mattes[$img1,$img2,1,32,Regular,0.25] \
    -t Affine[0.1] -c 50x40x30 \
    -f 4x2x1 -s 2x1x0 \
    -m CC[$img1,$img2,1,4] \
    -t SyN[0.25,3,0] -c 50x40x30 \
    -f 4x2x1 -s 2x1x0 -o $out
antsApplyTransforms -d $dim -i $img2 -o ${out}.nii.gz \
    -t ${out}1Warp.nii.gz -t ${out}0GenericAffine.mat -r $img1
CreateWarpedGridImage $dim ${out}1Warp.nii.gz \
    ${out}grid.nii.gz 1x1 10x10 10x10
```

# Mapping two images



Can vary smoothness, metrics, etc. See help.

# Segmenting anatomy with spatial priors

```
antsApplyTransforms -d 2 -i ${out}mk.nii.gz -o ${out}mk.nii.gz  
-t [${out}0GenericAffine.mat,1] -t ${out}1InverseWarp.nii.gz  
-n NearestNeighbor -r $img2  
antsApplyTransforms -d 2 -i ${out}prob0${x}.nii.gz \  
-o ${out}prob0${x}.nii.gz \  
-t [${out}0GenericAffine.mat,1] \  
-t ${out}1InverseWarp.nii.gz -n Linear -r $img2  
for x in 1 2 3 4 ; do  
    N4BiasFieldCorrection -d $dim -i $img2 -o ${out}.nii.gz \  
    -x ${out}mk.nii.gz -s 1 -b [200] -c [20x20x20,0] \  
    -w ${out}prob03.nii.gz  
    Atropos -d $dim -a ${out}.nii.gz -x ${out}mk.nii.gz \  
    -m [ 0.05,1x1] -c [10,0] \  
    -i priorprobabilityimages[3,${out}prob%02d.nii.gz,0.25] \  
    -o [${out}.nii.gz,${out}prob%02d.nii.gz]  
done
```

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What happens when i vary each parameter?

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- $-r \text{ Gauss}[6,3]$   $\$<\$ -r \text{ Gauss}[3,0]$
- Robustness increases with correlation window
- $-m \text{ CC}[\text{.}, \text{.}, 1, 4] < -m \text{ CC}[\text{.}, \text{.}, 1, 6]$

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- but computation time also increases

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- Details matter: pre-processing, feature extraction, etc.

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- Robustness increases with correlation window
- $-\text{m CC}[\text{.}, \text{.}, 1, 4] < -\text{m CC}[\text{.}, \text{.}, 1, 6]$
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- Details matter: pre-processing, feature extraction, etc.
- Successful affine step is essential!!

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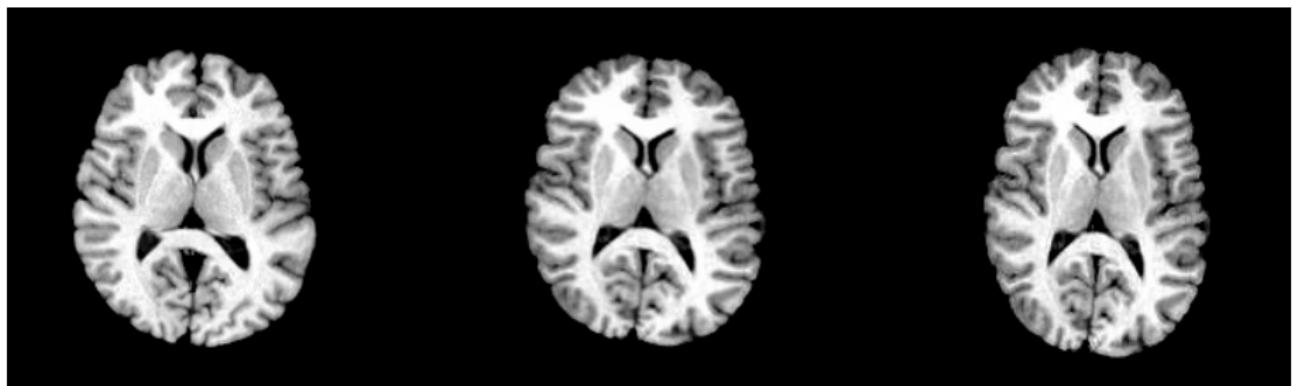
- Robustness increases with regularization
- $-r \text{ Gauss}[6,3]$   $\Rightarrow$   $-r \text{ Gauss}[3,0]$
- Flexibility decreases with regularization
- $-r \text{ Gauss}[6,3]$   $<$   $-r \text{ Gauss}[3,0]$
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- but computation time also increases
- Details matter: pre-processing, feature extraction, etc.
- Successful affine step is essential!!
- Step-size increases stability but slows convergence
- $SyN[0.1]$  more stable than  $SyN[0.25]$ .

# Check the affine mapping between two images



fixed versus affinely registered image versus original moving

# Coordinates of computation time

- 2D  $256^2$  pixels intensity difference (MSQ) registration  $\approx$  30 seconds

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- 2D  $256^2$  pixels intensity difference (MSQ) registration  $\approx$  30 seconds
- 3D  $256^3$  voxels correlation-8 ( CC[ . , . , 1, 8] ) could take 3 days if you use full-resolution and the images are very different.

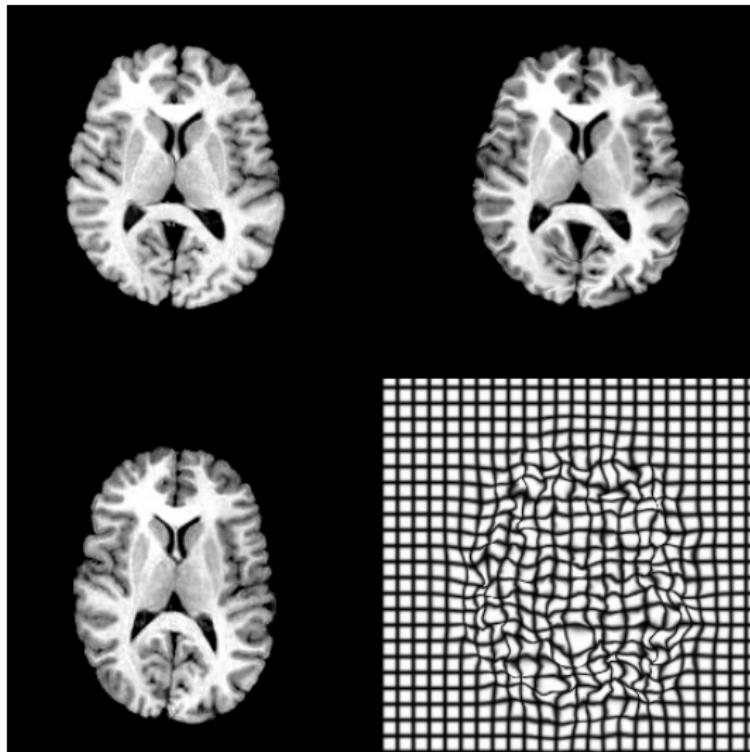
# Coordinates of computation time

- 2D  $256^2$  pixels intensity difference (MSQ) registration  $\approx$  30 seconds
- 3D  $256^3$  voxels correlation-8 ( CC[ . , . , 1, 8] ) could take 3 days if you use full-resolution and the images are very different.
- or it could take 15 minutes if you use low-resolution and the images are very similar.

# Multiple metrics driving registration

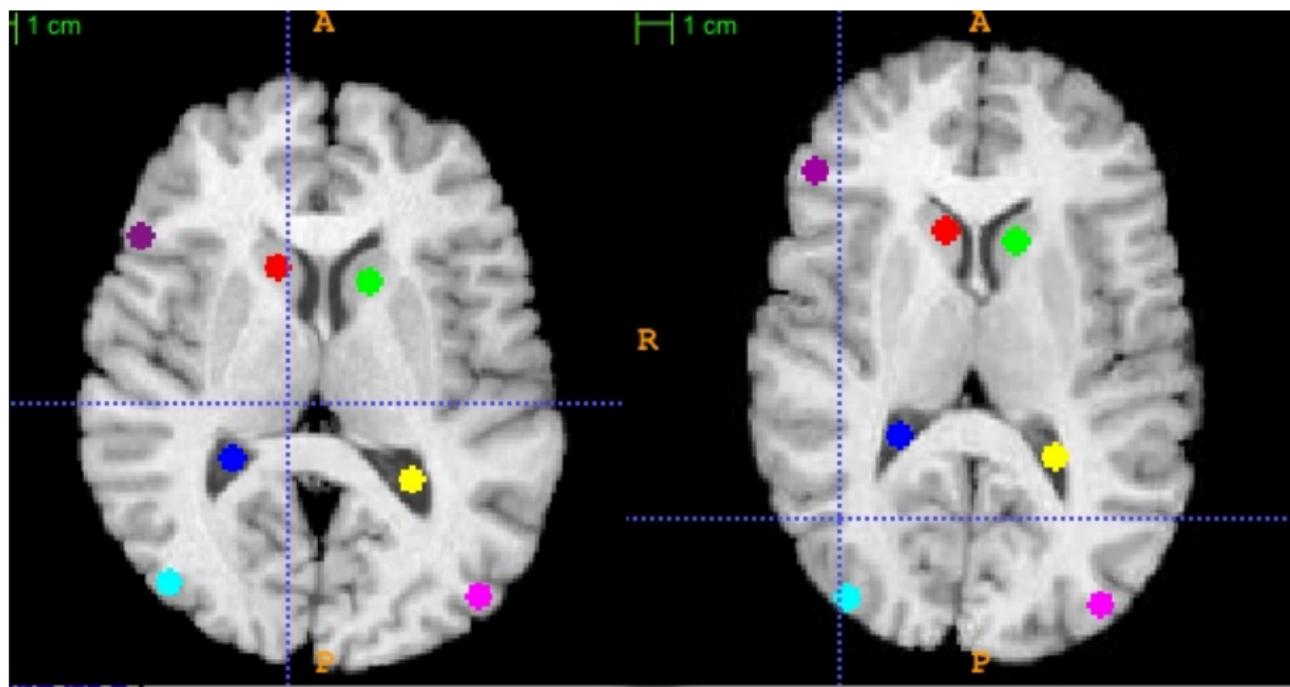
```
antsRegistration -d $dim -r [ $img1, $img2, 1 ] \
-m mattes[$img1,$img2,1,32,Regular,0.25] \
-t Affine[0.1] \
-c 50x40x30 \
-f 4x2x1 -s 2x1x0 \
-m CC[$img1,$img2,1,4] \
-m meansquares[$lm1,$lm2,1,4] \
-f 4x2x1 -s 2x1x0 \
-t SyN[0.25,3,0] -c 50x40x30 -o $out
```

# Multiple metrics driving registration



fixed versus ...

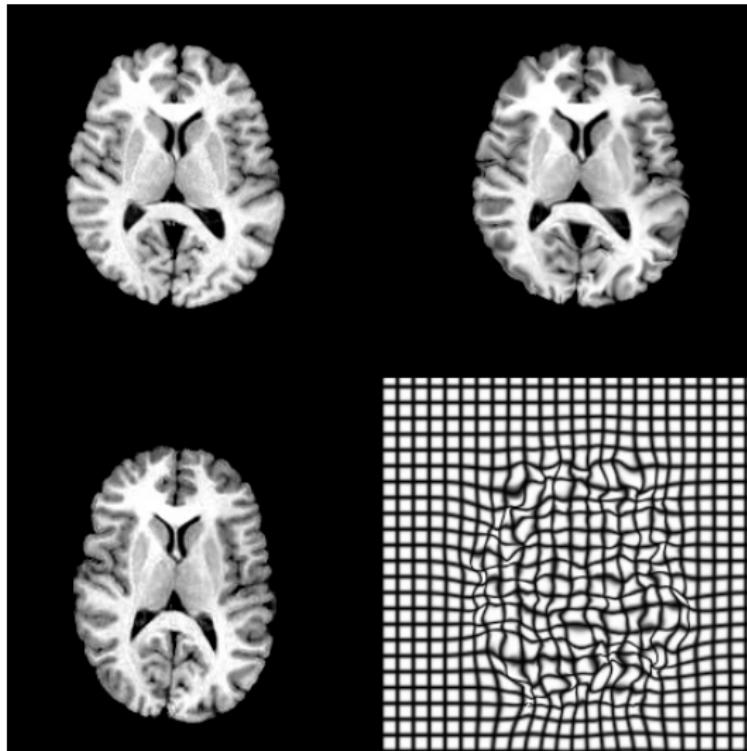
# Landmark-based registration 1



# Landmark-based registration 2

```
WarpImageMultiTransform $dim $lm2 ${out}lm.nii.gz \
${out}preAffine.txt -R $img1 --use-NN
WarpImageMultiTransform $dim $img2 ${out}img.nii.gz \
${out}preAffine.txt -R $img1
wt=1 ; pct=0.5 ; sig=50
ANTS $dim -i 55x40x30 -r Gauss[8,0] -t SyN[ 0.25 ]
-m PSE[ $lm1 , ${out}lm.nii.gz , $lm1 , ${out}lm.nii.gz
-m CC[$img1,${out}img.nii.gz,1,4] -o $out -i 50x50x50 --num
--use-all-metrics-for-convergence 1 --continue-affine 0
```

# Landmark-based registration 3



# Other Landmark-based registration tools

- for 3D

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- for 3D
- ANTSUseLandmarkImagesToGetAffineTransform Im1.nii.gz Im2.nii.gz  
affine outaffine.txt

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- for 3D
- ANTSUseLandmarkImagesToGetAffineTransform Im1.nii.gz Im2.nii.gz  
affine outaffine.txt
- ANTSUseLandmarkImagesToBSplineDisplacementField Im1.nii.gz  
Im2.nii.gz outLMWarp.nii.gz 10x10x10 6 3 0

# Other Landmark-based registration tools

- for 3D
- ANTSUseLandmarkImagesToGetAffineTransform Im1.nii.gz Im2.nii.gz  
affine outaffine.txt
- ANTSUseLandmarkImagesToBSplineDisplacementField Im1.nii.gz  
Im2.nii.gz outLMWarp.nii.gz 10x10x10 6 3 0
- Then use WarpImageMultiTransform / antsApplyTransform to apply  
the warp to the relevant image.

# Template based studies

# Template construction

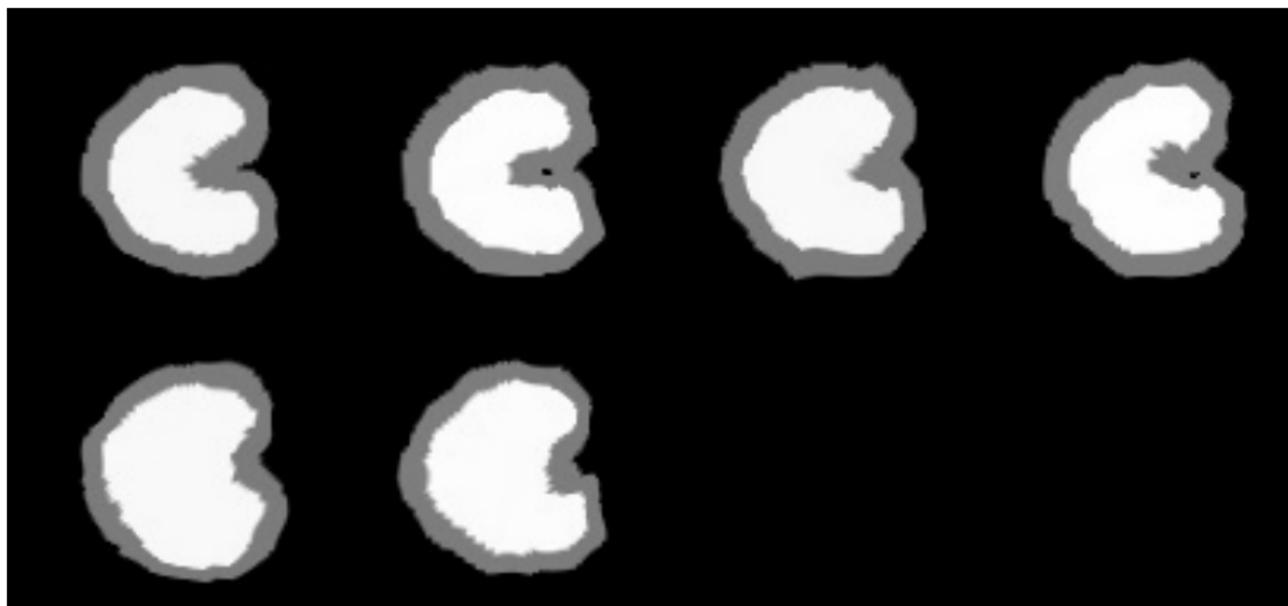
```
ln -s ./data/phantom* .
buildtemplateparallel.sh -d 2 -o PH -c 0 \
    -s CC -i 3 -m 50x0x0 -t GR phantom*.jpg
```

# Template construction



all “subjects”

# Template construction output



subjects after iteration 1

# Template construction output



subjects after iteration 2

# Multi-template labeling

```
for x in *deformed.nii.gz ; do
    Atropos -d 2 -a $x -m [0.1,1x1] -i kmeans[2] \
    -x mask.nii.gz -o [temp${ct}seg.nii.gz] -c [3,0]
ls temp*seg.nii.gz > list.txt
ImageSetStatistics 2 list.txt PHtemplateseg.nii.gz 0
```

# Multi-template labeling



The template and its groupwise segmentation.

# Population statistics

# Identifying local predictors of global differences

$$\text{volume}_{\text{local}} \approx 1 + \text{volume}_{\text{global}}$$

# ANTs multivariate voxel-wise statistics

```
phseg=antsImageRead( paste(bd,"PHtemplateseg.nii.gz",sep=''))  
mask=thresholdImage( phseg, 1, 1 )  
jlist=list()  
for ( x in Sys.glob( paste(bd,"PH*mWarp.nii.gz",sep='')) ) {  
  jac = createJacobianDeterminantImage(mask,x,1)  
  jlist = lappend( jlist, jac %>% smoothImage(0.5) )  
}  
mat=imageListToMatrix( jlist, mask )
```

# ANTs multivariate voxel-wise statistics

```
mats=list( mat, cbind( dx, predictor2 ) )
sccaner=sparseDecom2( mats, c(mask,NA),
  sparseness = c( 0.2, -1 ),
  nvecs=2, its=10, perms=200,
  cthresh=c(50,0), mycoption = 0 )
print( sccaner$ccasummary )
```

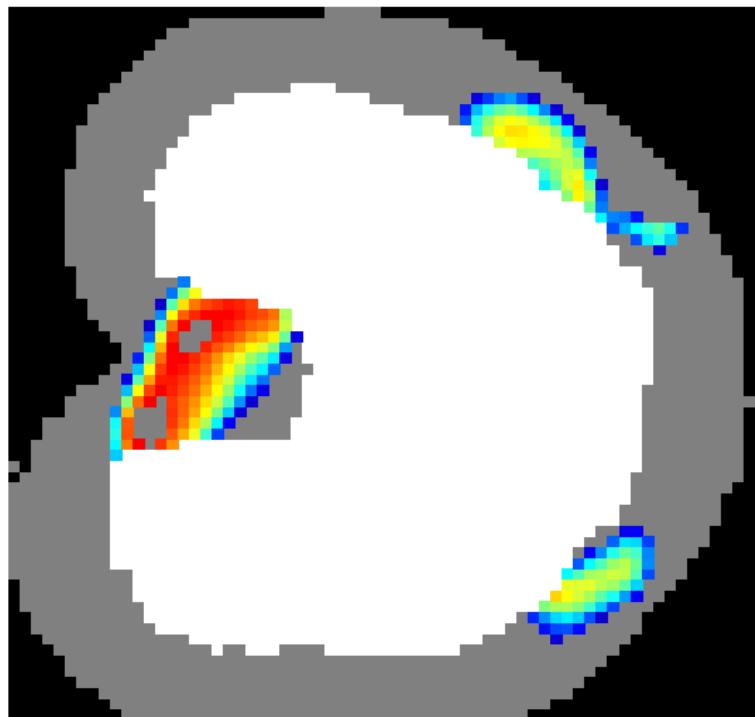
```
##      TypeOfMeasure Variate000 Variate001 x
## 1 final_p_values  0.00497512   0.278607 x
## 2             corrs  0.97428100   0.430848 x
```

```
print( sccaner$eig2 )
```

```
##      Variate000 Variate001
## 1 -0.1861912 -1.139789
## 2  0.1972314 -1.075988
```

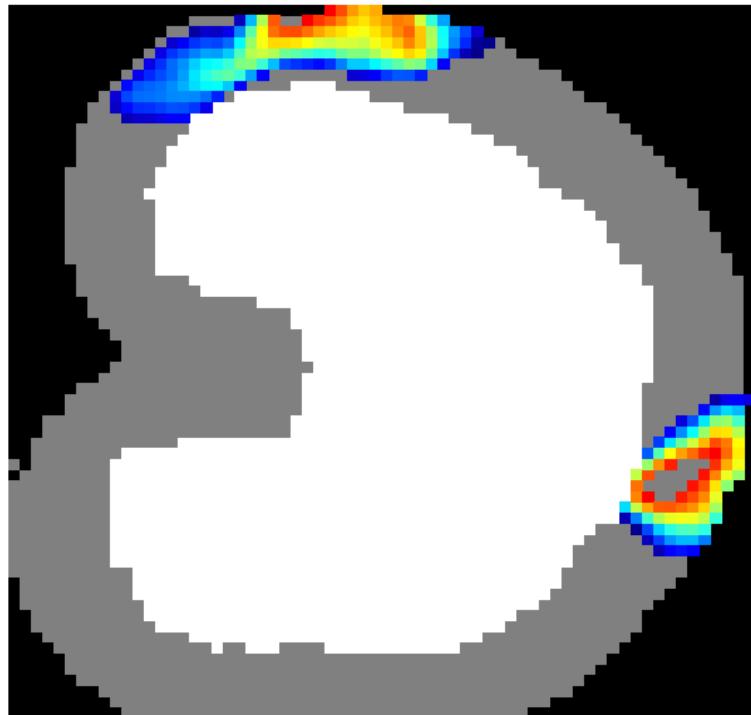
# ANTs multivariate voxel-wise statistics

```
plot( phseg, sccaner$eig1[[1]] , window.img=c(0,Inf))
```



# ANTs multivariate voxel-wise statistics

```
plot( phseg, sccaner$eig1[[2]] , window.img=c(0,Inf))
```



# .... voxel-wise statistics in R

```
lmres<-lm( mat ~ dx + predictor2 )
blmres=bigLMStats( lmres )
pvals1=blmres$beta.pval[1,]
qvals1<-p.adjust(pvals1,'BH')
pvals2=blmres$beta.pval[2,]
qvals2<-p.adjust(pvals2,'BH')
print( paste( min( qvals1 ) , min( qvals2 ) ) )
```

```
## [1] "0.656351348427606 0.032058087370388"
```

# .... voxel-wise statistics in *R*

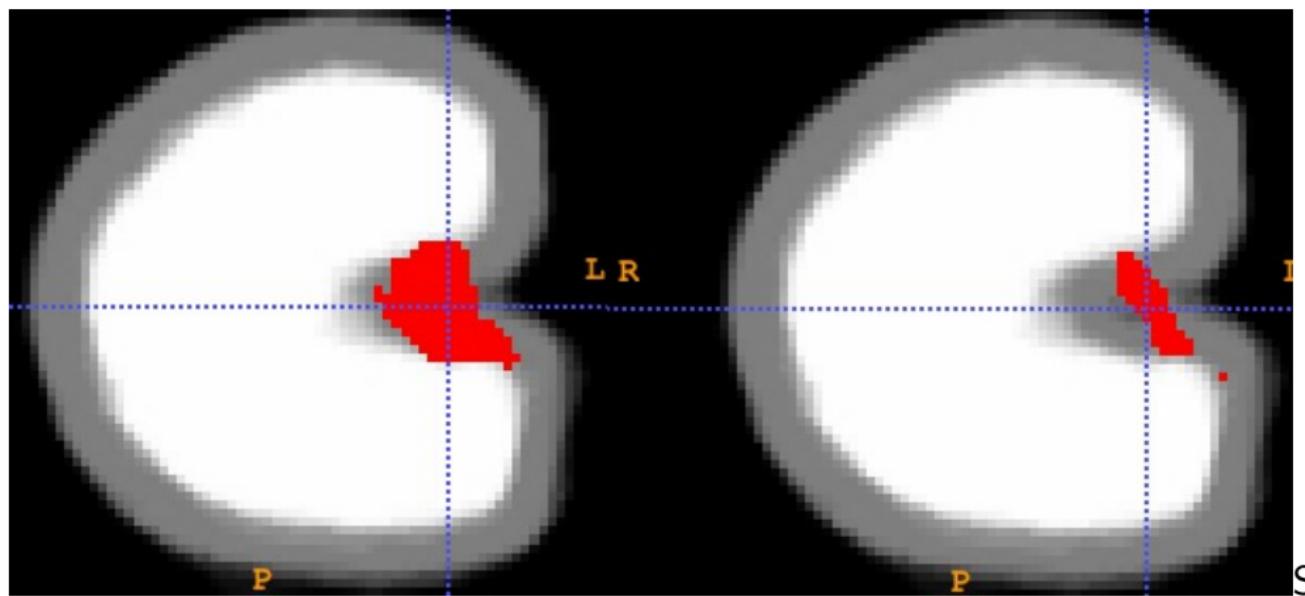


# .... voxel-wise statistics in R

```
lmres<-lm( mat ~ dx + predictor2 + rowMeans(mat) )
blmres=bigLMStats( lmres )
pvals1=blmres$beta.pval[1,]
qvals1<-p.adjust(pvals1,'BH')
pvals2=blmres$beta.pval[2,]
qvals2<-p.adjust(pvals2,'BH')
print( paste( min( qvals1 ) , min( qvals2 ) ) )
```

```
## [1] "0.604600838470526 0.179937670859169"
```

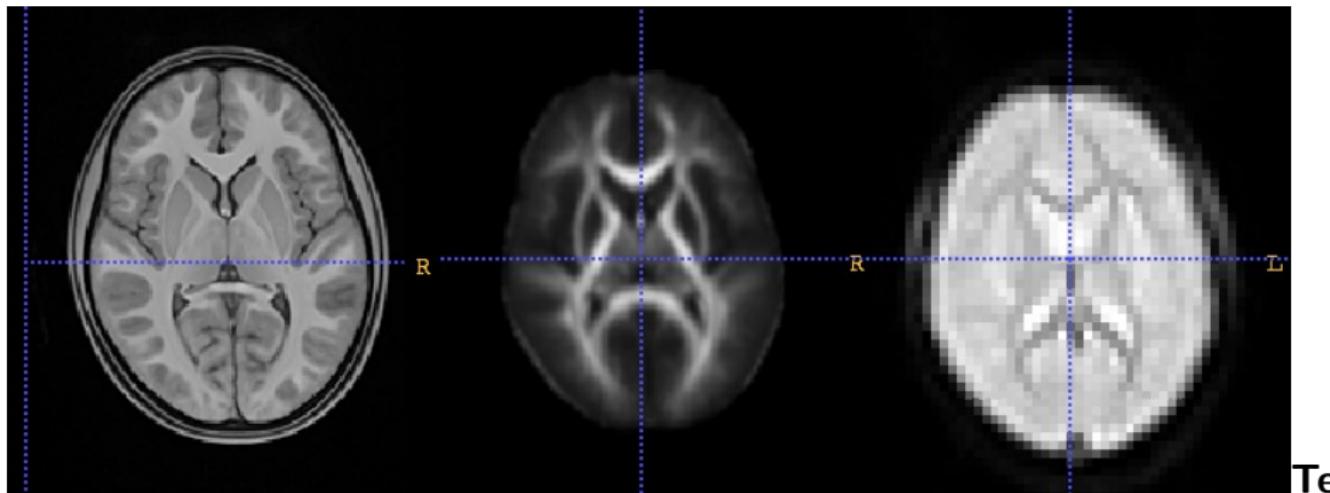
# Comparison of results



$p$ -value  $\approx 0.003$  minimum FDR-corrected  $p$ -value  $\approx 0.009$  but results are similar. FDR threshold = 0.05.

# Multiple modality processing

# Templates for all modalities



for the same population T1, FA and BOLD.

We exploit population templates to extract the brain and set-up modality specific brain extraction and segmentation.

# Longitudinal analysis with ANTs

Look at your data to verify the quality of the rigid mapping!

# Processing of diffusion tensor data.

- Intra-subject matching (  $T1 \rightarrow FA$  )

# Processing of diffusion tensor data.

- Intra-subject matching (  $T1 \rightarrow FA$  )
- Compose warps for template space warp

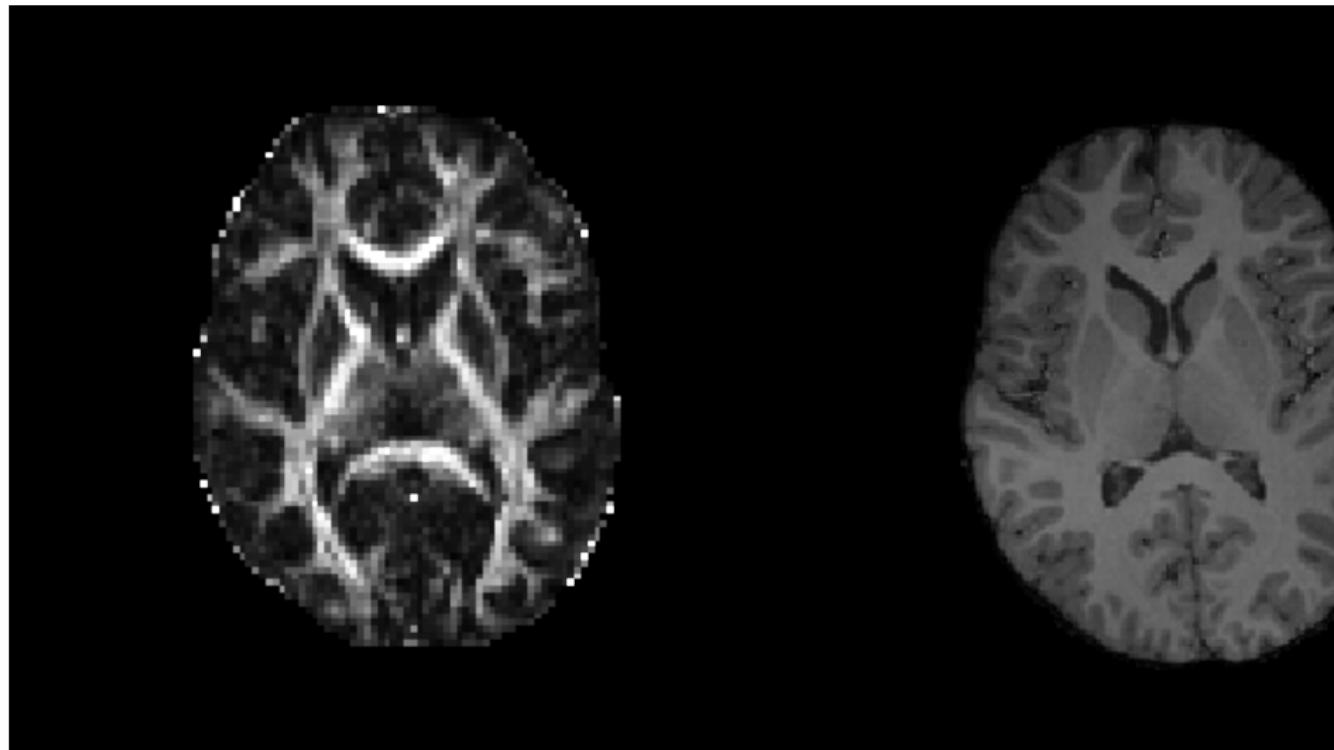
# Processing of diffusion tensor data.

- Intra-subject matching (  $T1 \rightarrow FA$  )
- Compose warps for template space warp
- Warp and reorient with preservation of principal direction

# Processing of diffusion tensor data.

- Intra-subject matching (  $T1 \rightarrow FA$  )
- Compose warps for template space warp
- Warp and reorient with preservation of principal direction
- Get derived images (FA, MD, RGB, etc)

## Processing of diffusion tensor data.



FA & Subject T1 & Aligned composite

# Time series / rsfMRI analysis with ANTs

```
antsMotionCorr -d 3 -a $img -o ${out}avg.nii.gz
antsMotionCorr -d 3 -o [${out}, ${out}.nii.gz, ${out}avg.nii.gz]
-m mi[ ${out}avg.nii.gz , $img , 1 , 32 , Regular, 0.05 ]
-t Rigid[ 0.5 ] -i 25 -u 1 -e 1 -s 0.0 -f 1 -n 10
```

# Time series / rsfMRI analysis with ANTs

- mi — mutual information metric

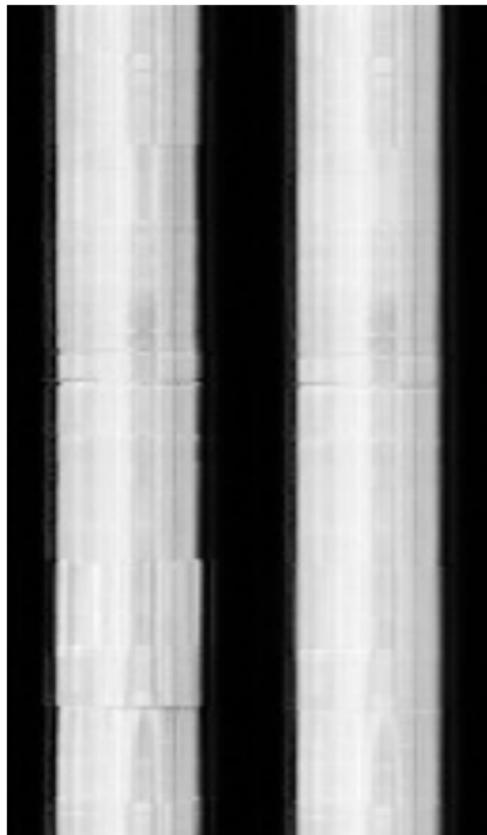
# Time series / rsfMRI analysis with ANTs

- mi — mutual information metric
- Rigid — use rigid map to the average with gradient step 0.05

# Time series / rsfMRI analysis with ANTs

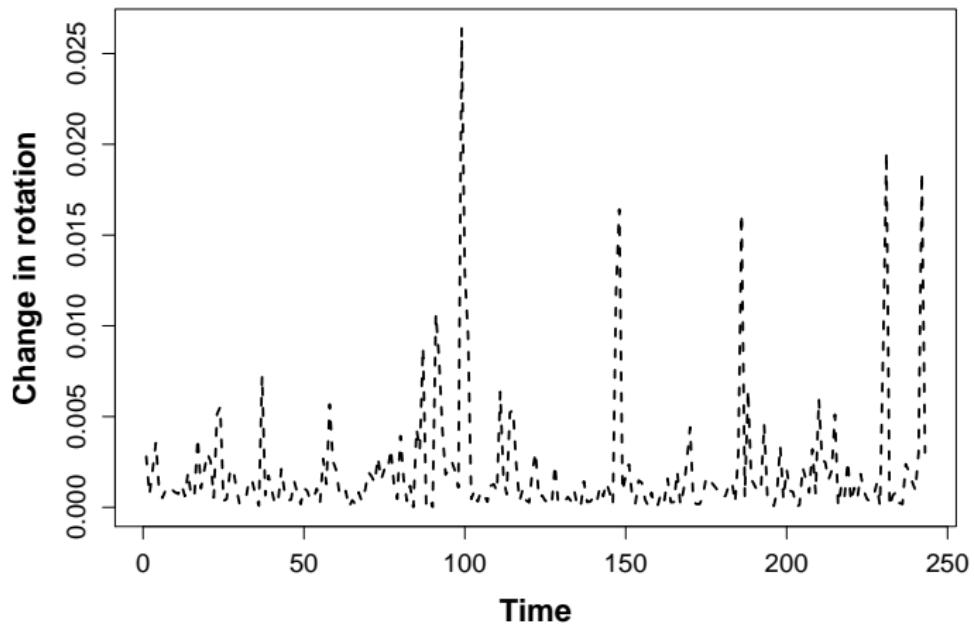
- mi — mutual information metric
- Rigid — use rigid map to the average with gradient step 0.05
- other params — smoothing, scale estimation, iterations . . .

# Time series / rsfMRI analysis with ANTs

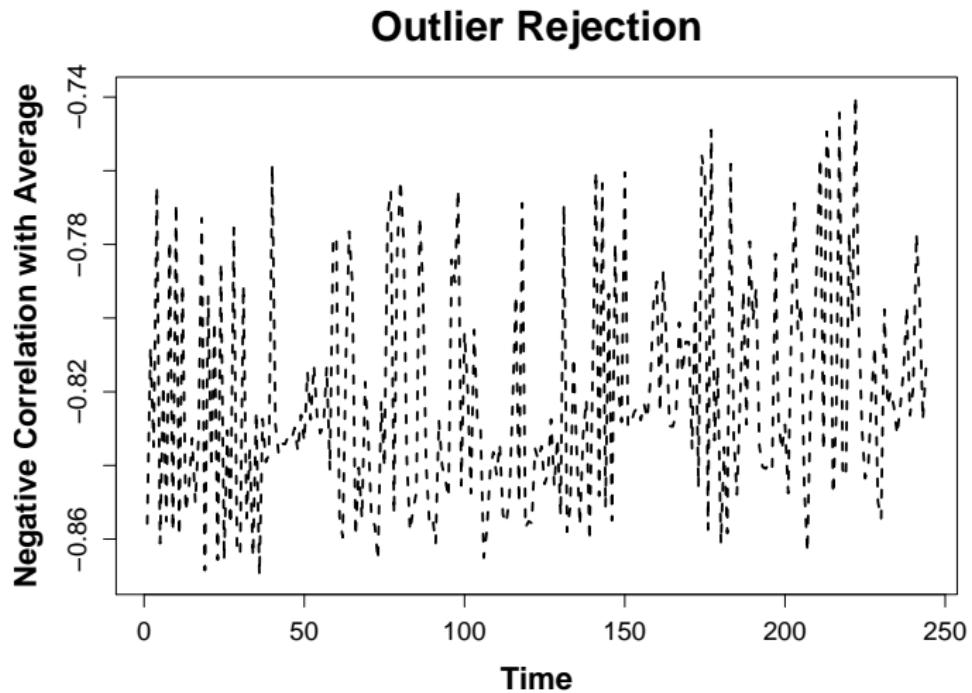


# Time series / rsfMRI analysis with ANTs

## Outlier Rejection



# Time series / rsfMRI analysis with ANTs}



# Extracting a resting state network

```
ThresholdImage 3 ${out}avg.nii.gz ${out}_bmask.nii.gz 300 999  
ImageMath 3 ${out}_bmask.nii.gz GetLargestComponent ${out}_bma  
ImageMath 4 ${out}compcorr.nii.gz CompCorrAuto \  
 ${out}.nii.gz ${out}_bmask.nii.gz 6  
sccan --timeseriesimage-to-matrix \  
 [ ${out}compcorr_corrected.nii.gz , ${out}_bmask.nii.gz ,  
 -o ${out}.csv  
sccan --svd recon[ ${out}.csv , ${out}_bmask.nii.gz , 0.05 ]  
 --l1 1 -n 20 -i 10 --PClusterThresh 50 -o ${out}RSFNodes.nii
```

Then build a graph ( see iGraph ).

# How does structure and functional connectivity elaborate during development?

open data

# Reproducibility

- ANTs is ideal for producing reproducible research.

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- ANTs is ideal for producing reproducible research.
- It is multi-platform and portable.
- It can easily be modified for + + + different types of studies.

# Reproducibility

- ANTs allows one to access the powers of both ITK and *R*.

## Reproducibility

- ANTs allows one to access the powers of both ITK and *R*.
- We aim to support user needs so if you can't find something, just ask . . . Questions?

# Acknowledgements

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