

Brain Image Analysis with  
SPM (VBM) and Freesurfer

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# Outline

- **Voxel-Based Morphometry**
  - Sequence of processes
  - 1. Co-registration
  - 2. Segmentation
  - 3. DARTEL
  - 4. Normalization
  - 5. Stats
- **Freesurfer**
  - Recon-all
  - Segmentation
  - results



# Measuring differences with MRI

- What are the significant differences between populations of subjects?
- What effects do various genes have on the brain?
- What changes occur in the brain through development or aging?
- A significant amount of the difference (measured with MRI) is anatomical.

# Voxel-Based Morphometry

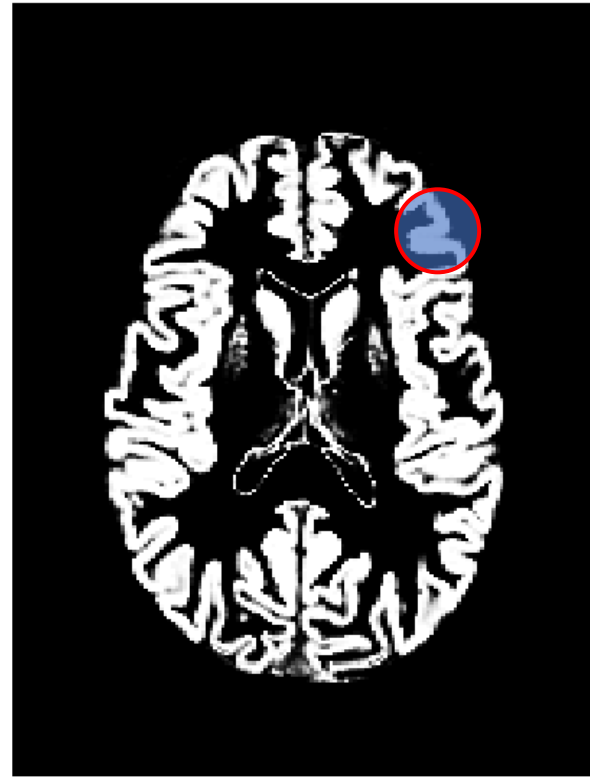
- Based on comparing regional volumes of tissue.
- Produce a map of statistically significant differences among populations of subjects.
  - e.g. compare a patient group with a control group.
  - or identify correlations with age, test-score etc.
- The data are pre-processed to sensitise the tests to regional tissue volumes.
  - Usually grey or white matter.
- Suitable for studying focal volumetric differences of grey matter.



# Volumetry



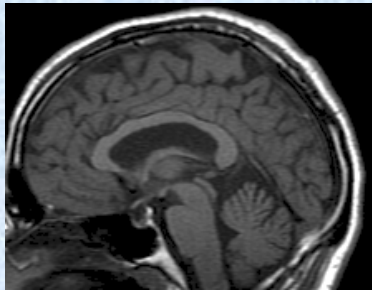
T1-Weighted MRI



Grey Matter

# SPM for Anatomical

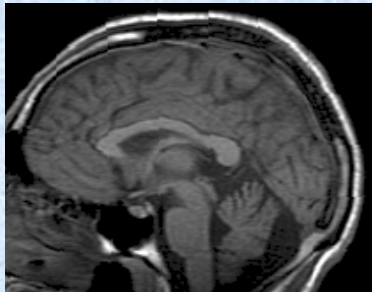
Anatomical MRI



Preprocessing

Spatially Normalised  
Grey Matter Image

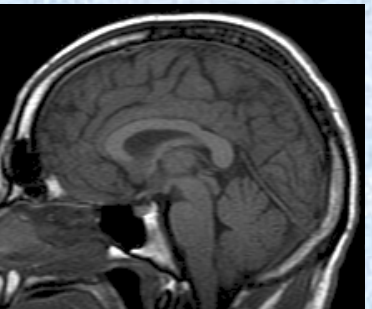
Anatomical MRI



Preprocessing

Spatially Normalised  
Grey Matter Image

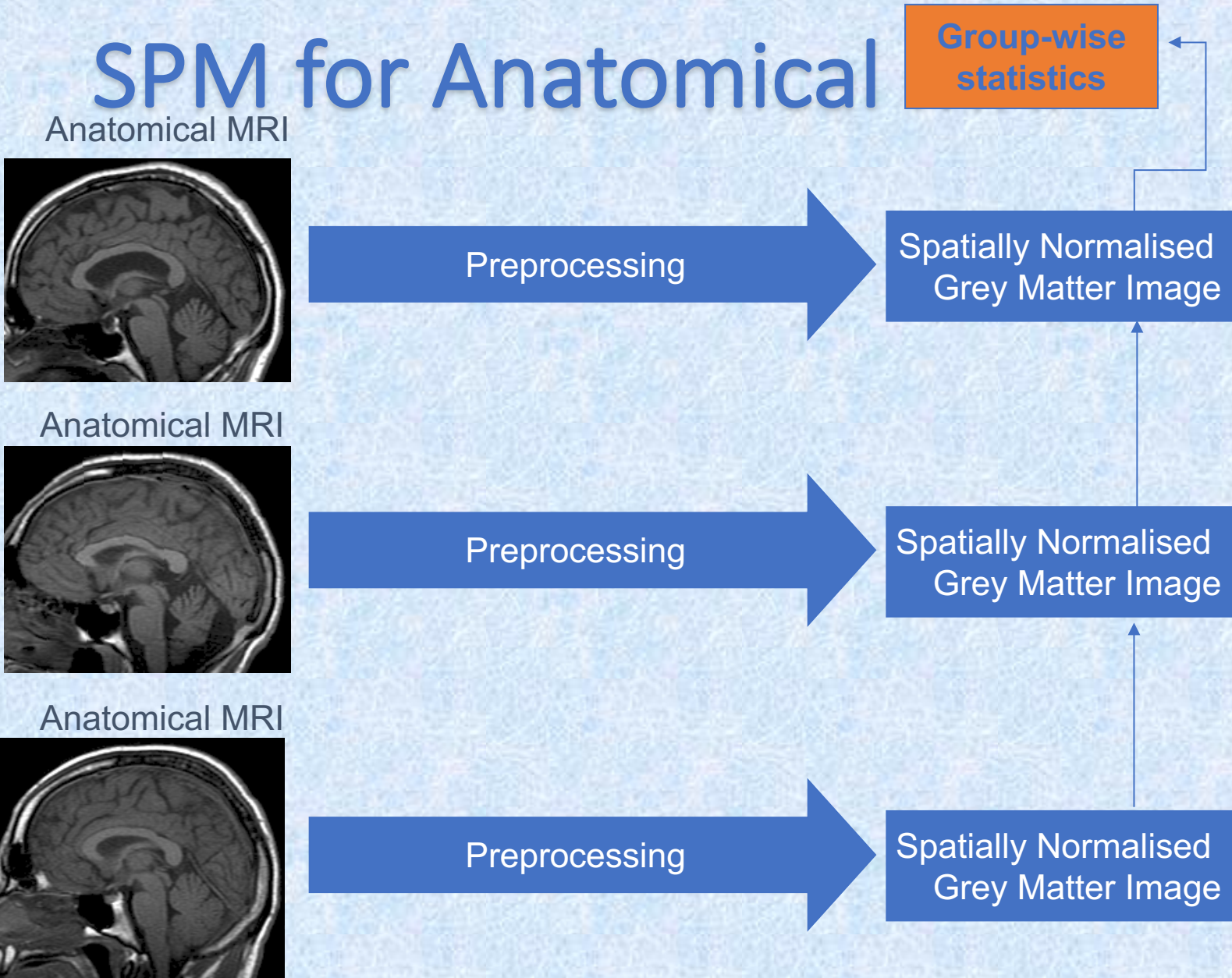
Anatomical MRI



Preprocessing

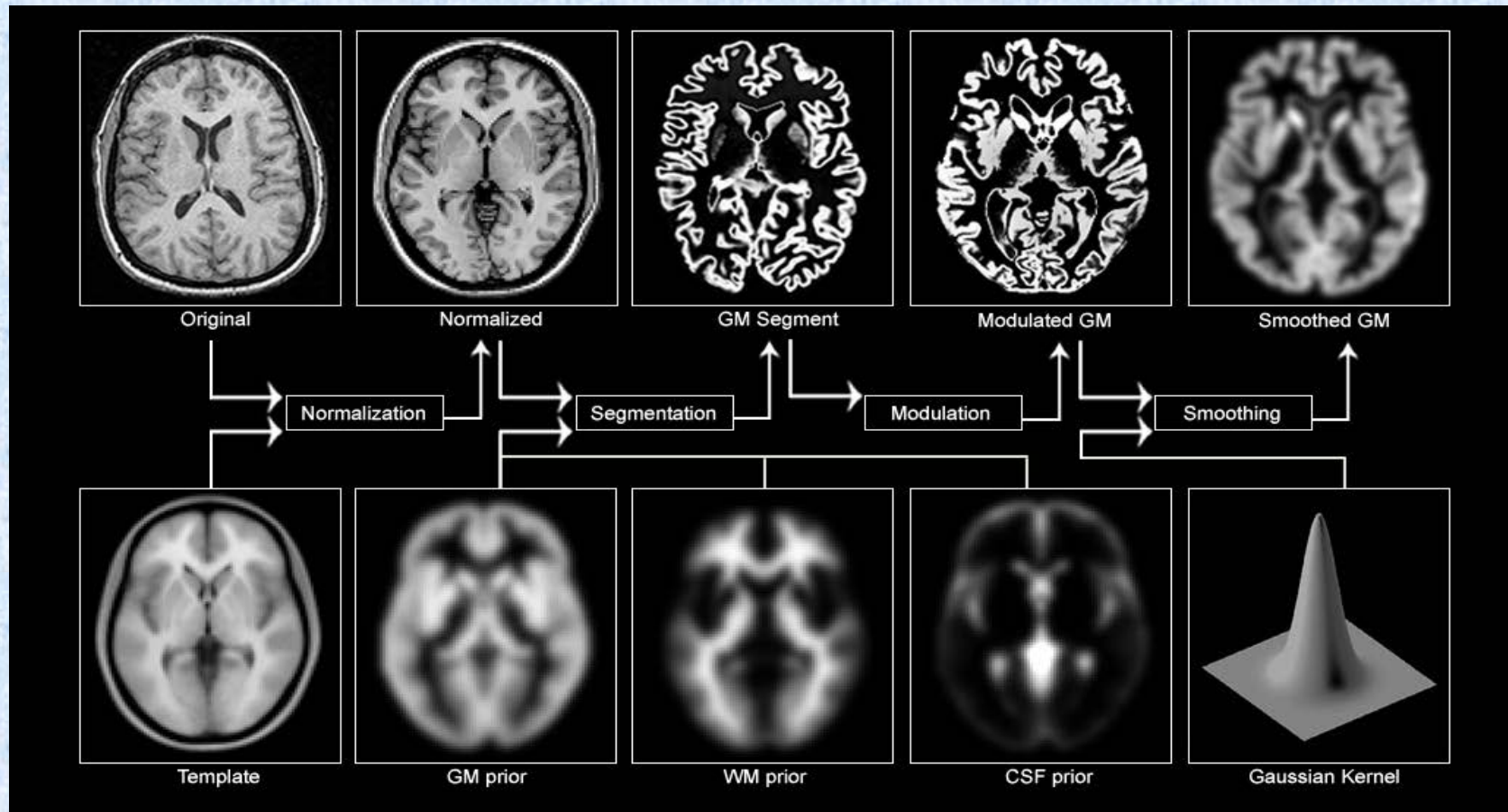
Spatially Normalised  
Grey Matter Image

Group-wise  
statistics





# Voxel-based morphometry – preprocessing overview



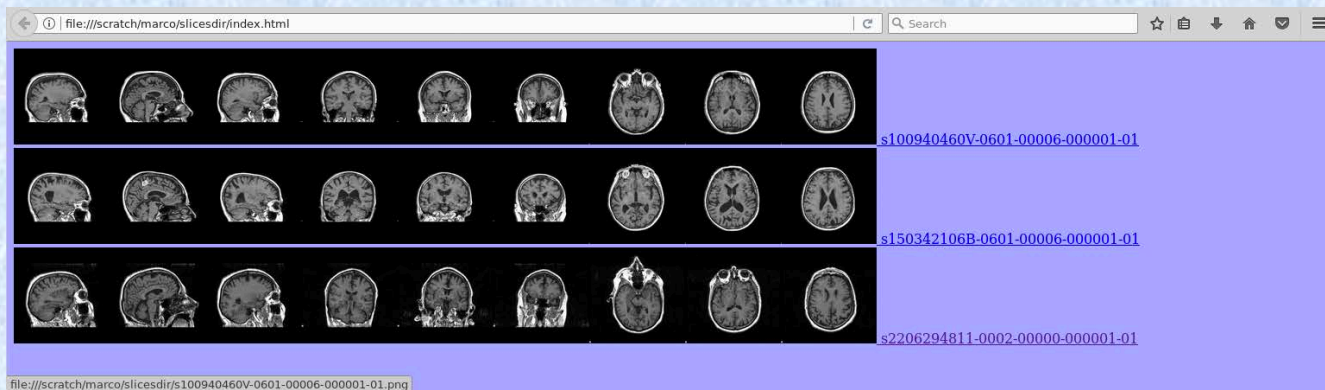
# VBM (Procedure in SPM 12)

Requires MATLAB (Commercial software)

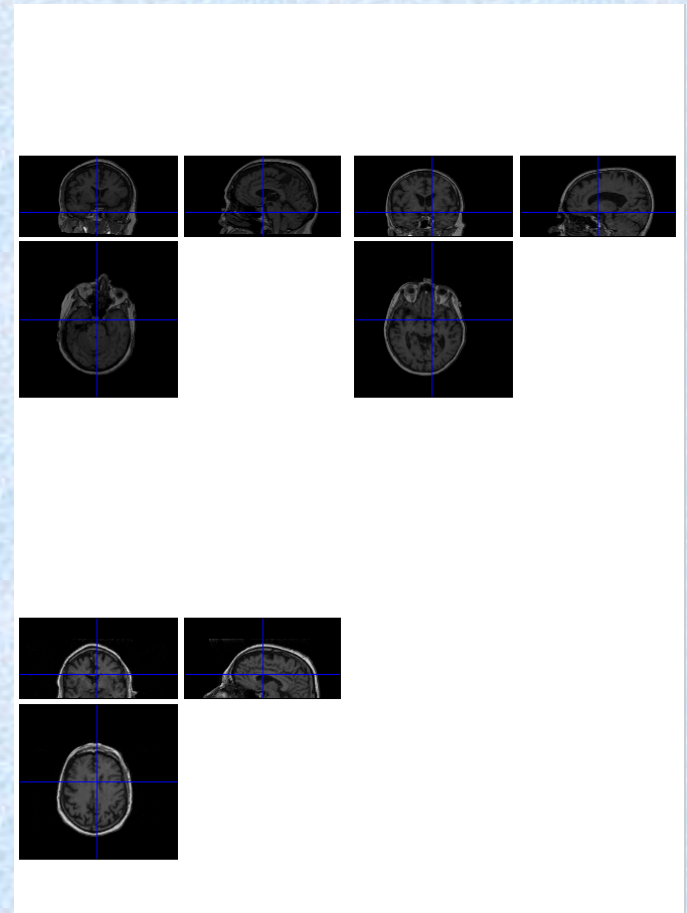
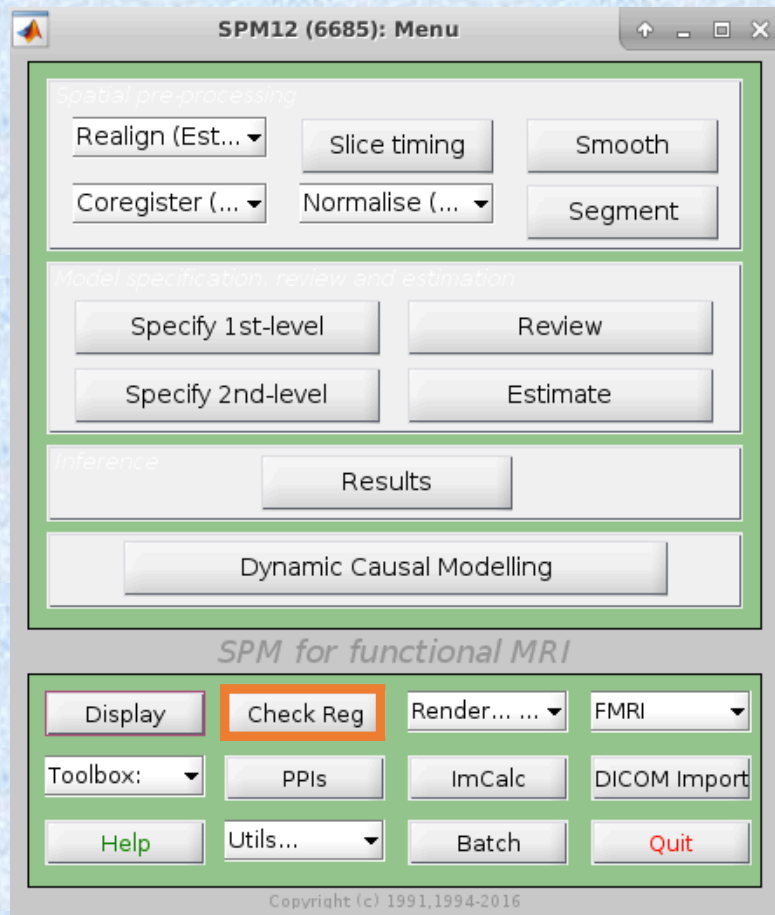


# SPM Dartel VBM analysis (1)

- INPUT IMAGE FILE FORMAT: NIFTI (.nii)
  - (SPM can import a various of file formats, like DICOM)
- Quality check of the images using Freesurfer's "slicesdir"
  - Working Folder with all images to process > slicesdir \*.nii
  - Inspect Working Folder\slicesdir\index.html

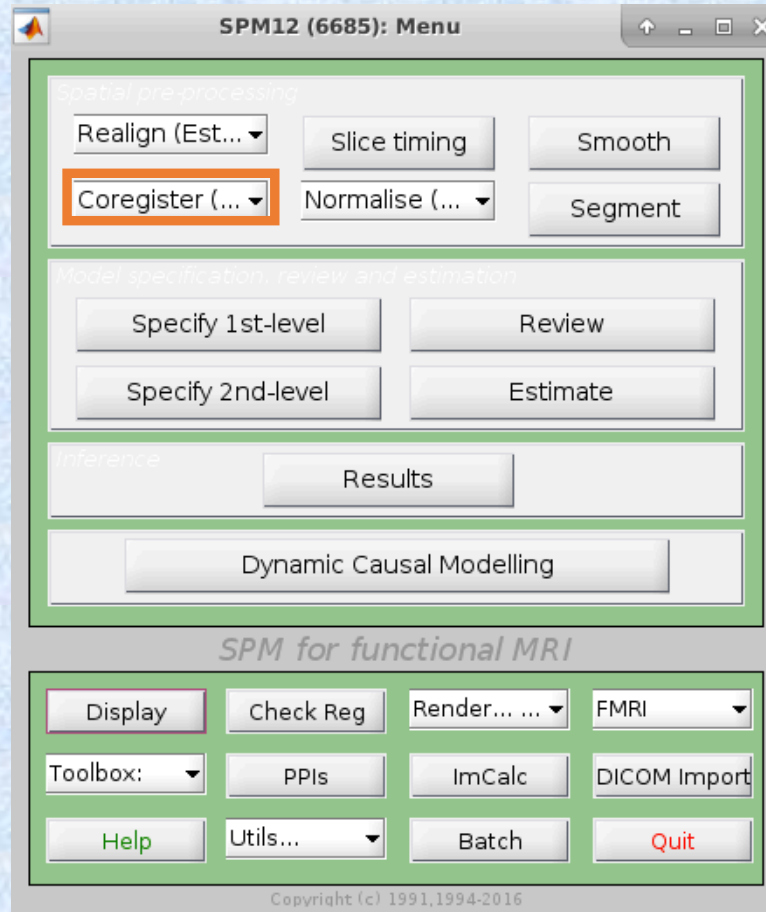


# Check Reg – Inspect multiple images



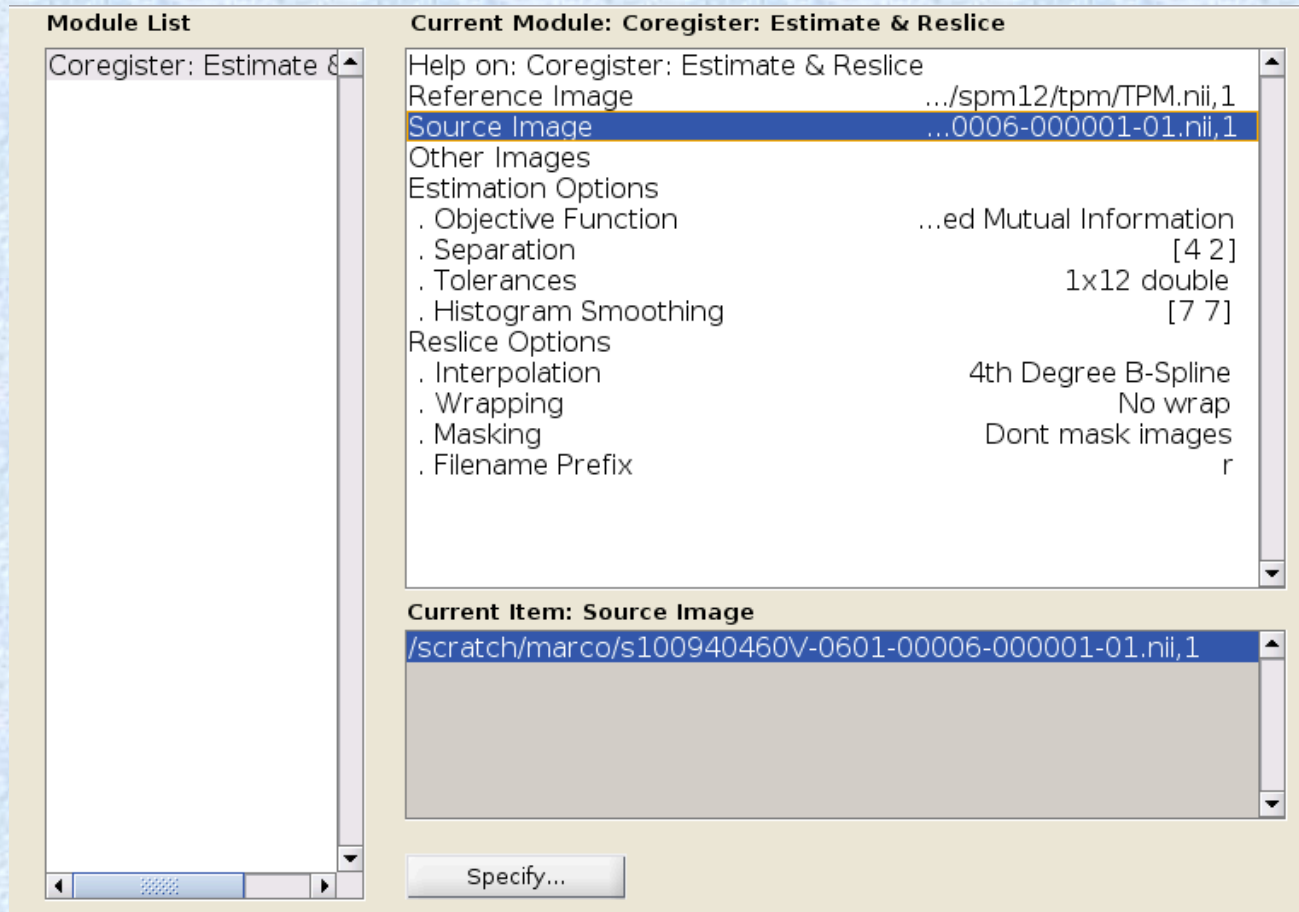


# 1. Coregister (estimate and reslice (3<sup>rd</sup> option))

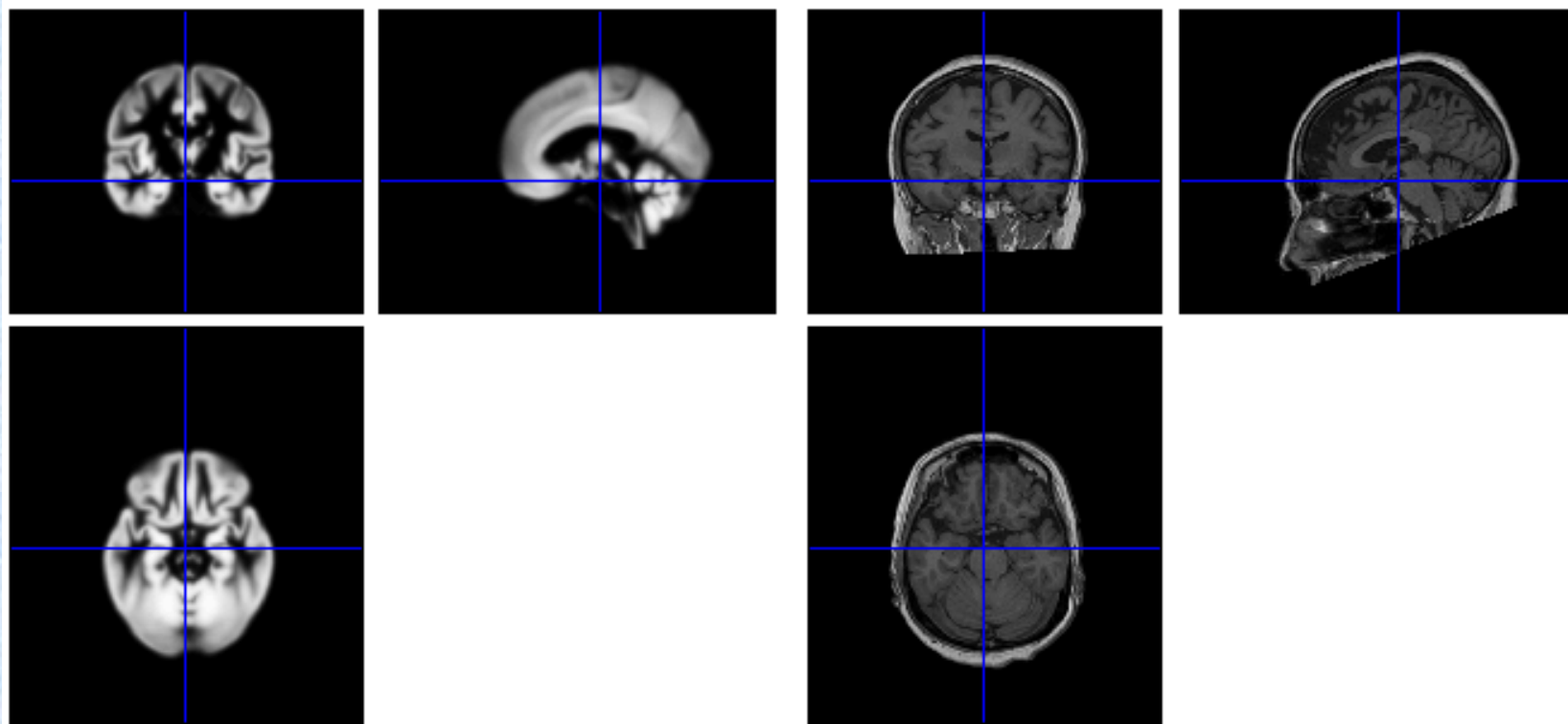


# Select TPM Template as Reference

## Select NIFTI (T1W MRI) as Source

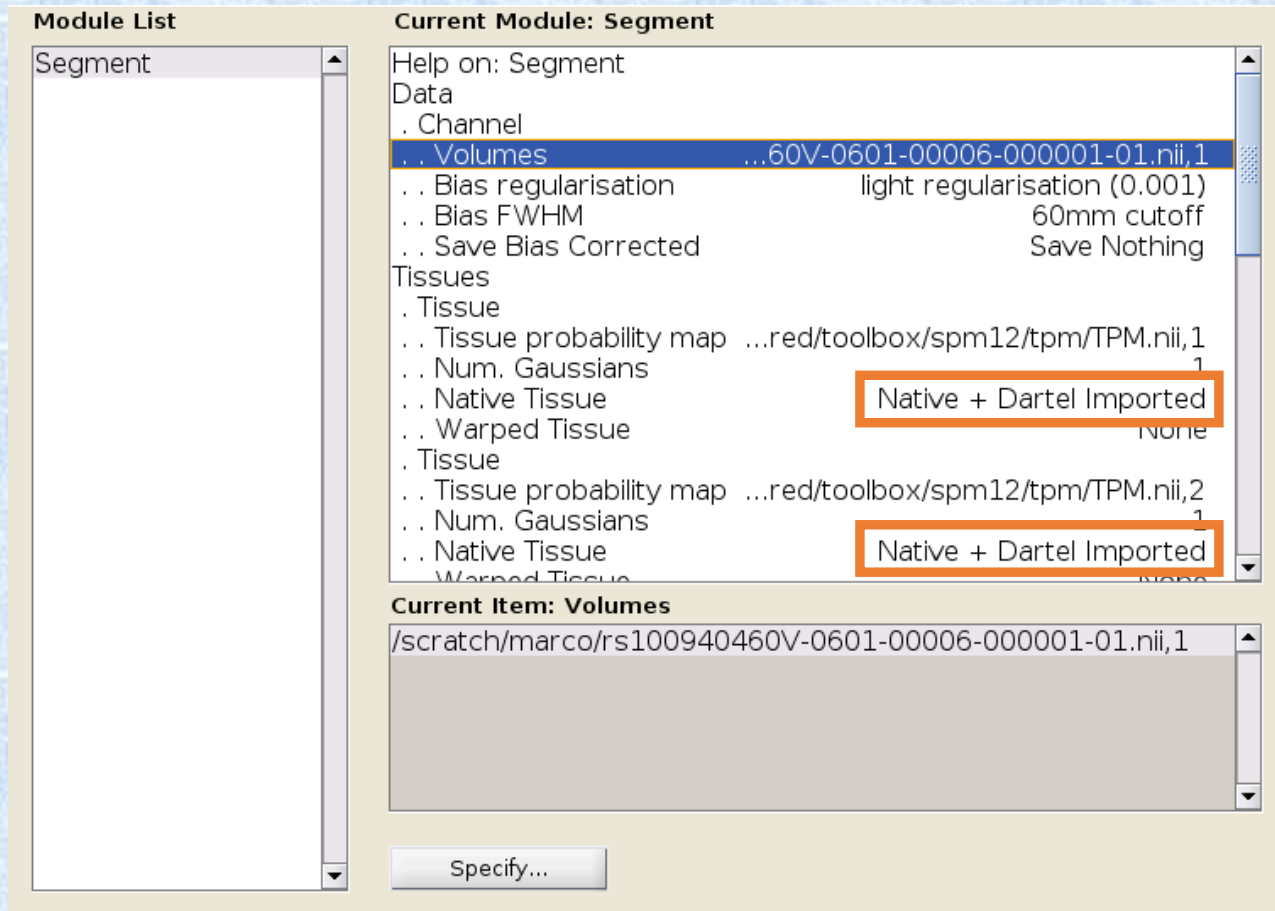


# After coregistration (rFilename.nii)

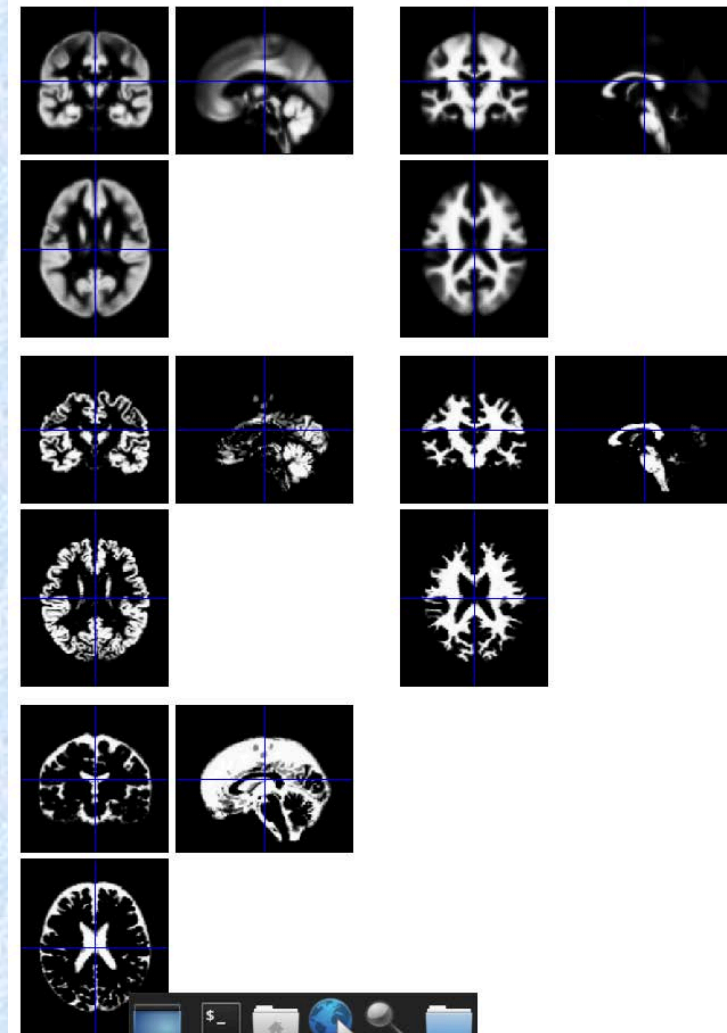
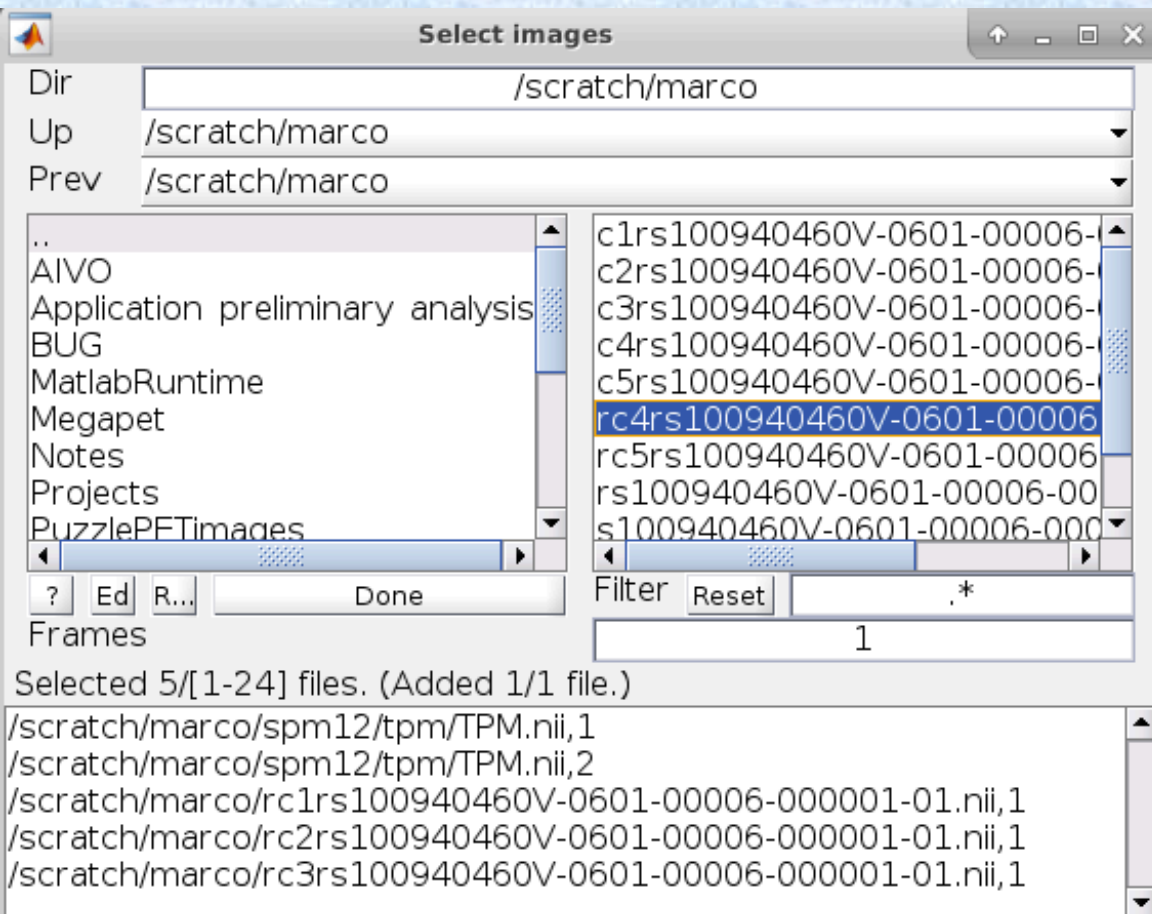




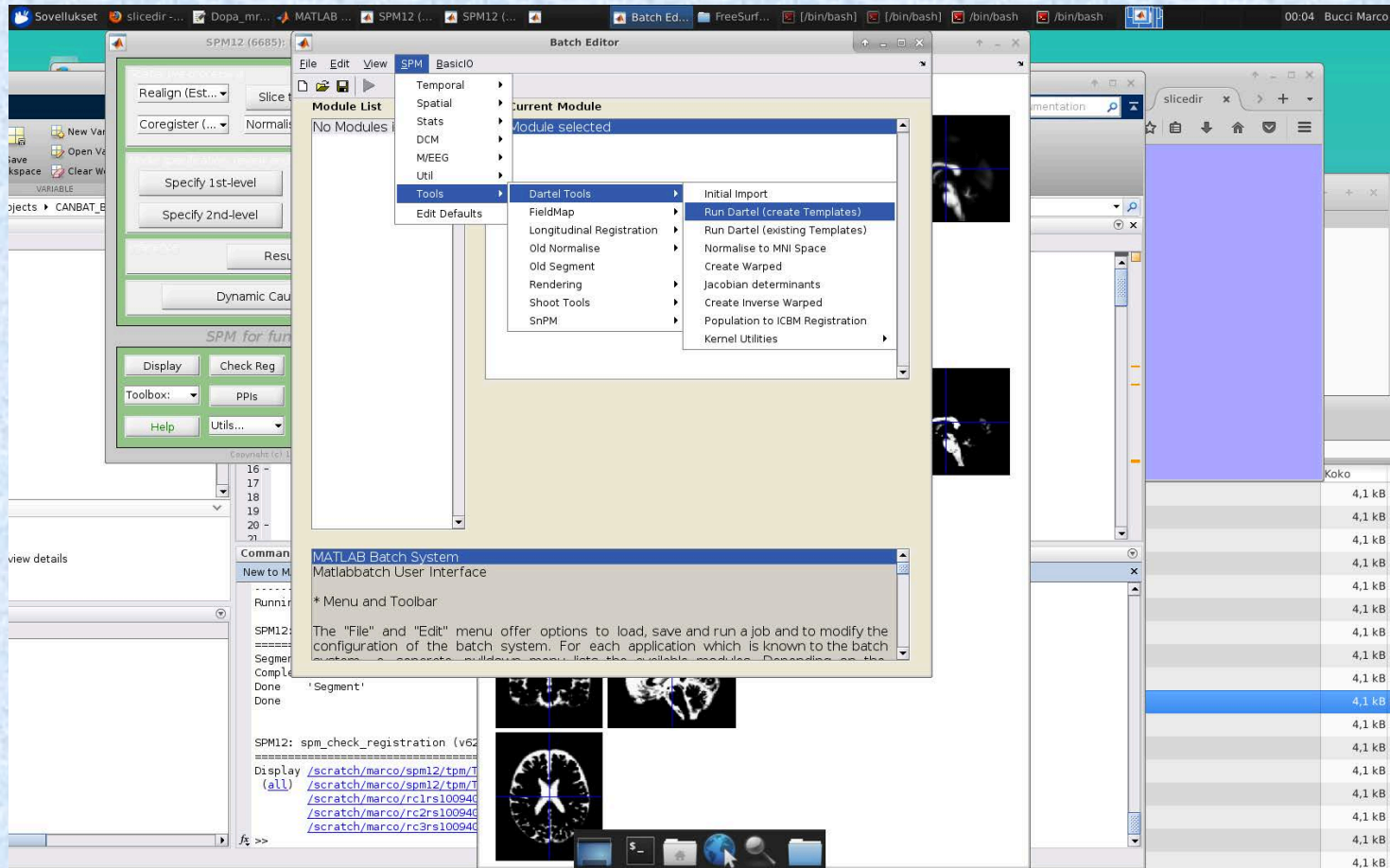
## 2. Segment (From SPM menu) Select rFilename as Volumes



# Check Reg results (Binary images, unwarped)



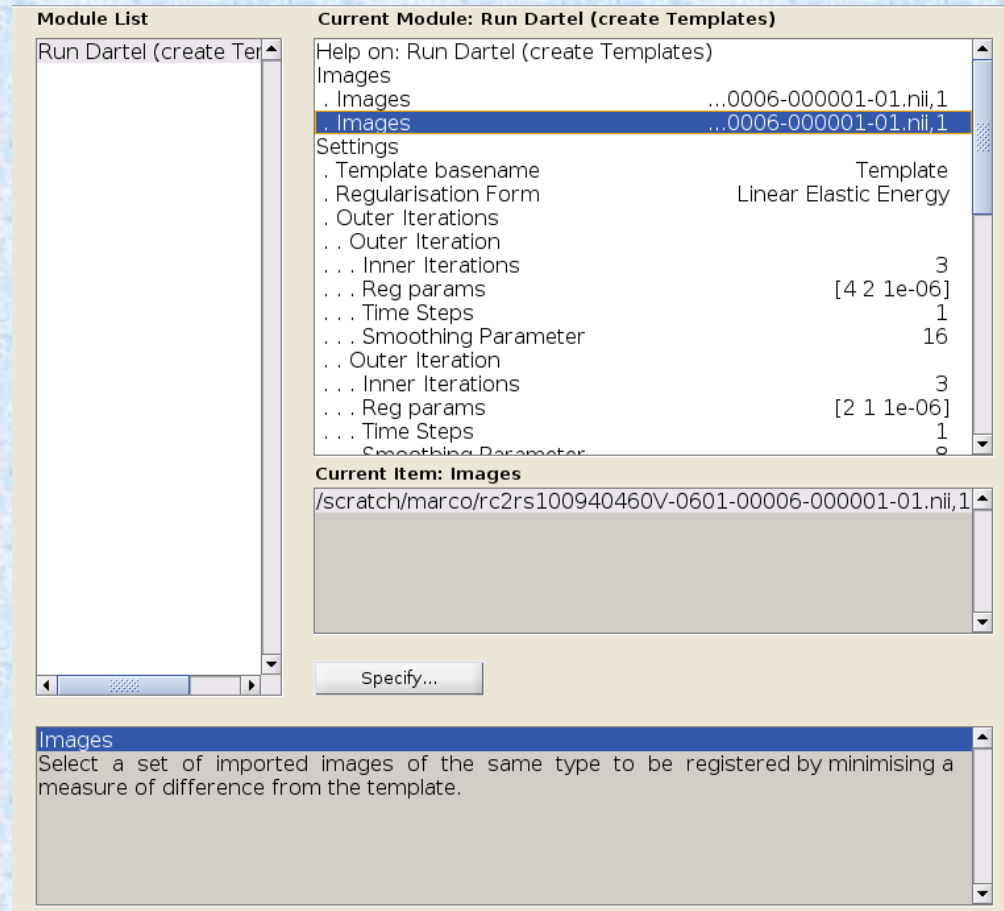
# 3. Run Dartel (create Template)



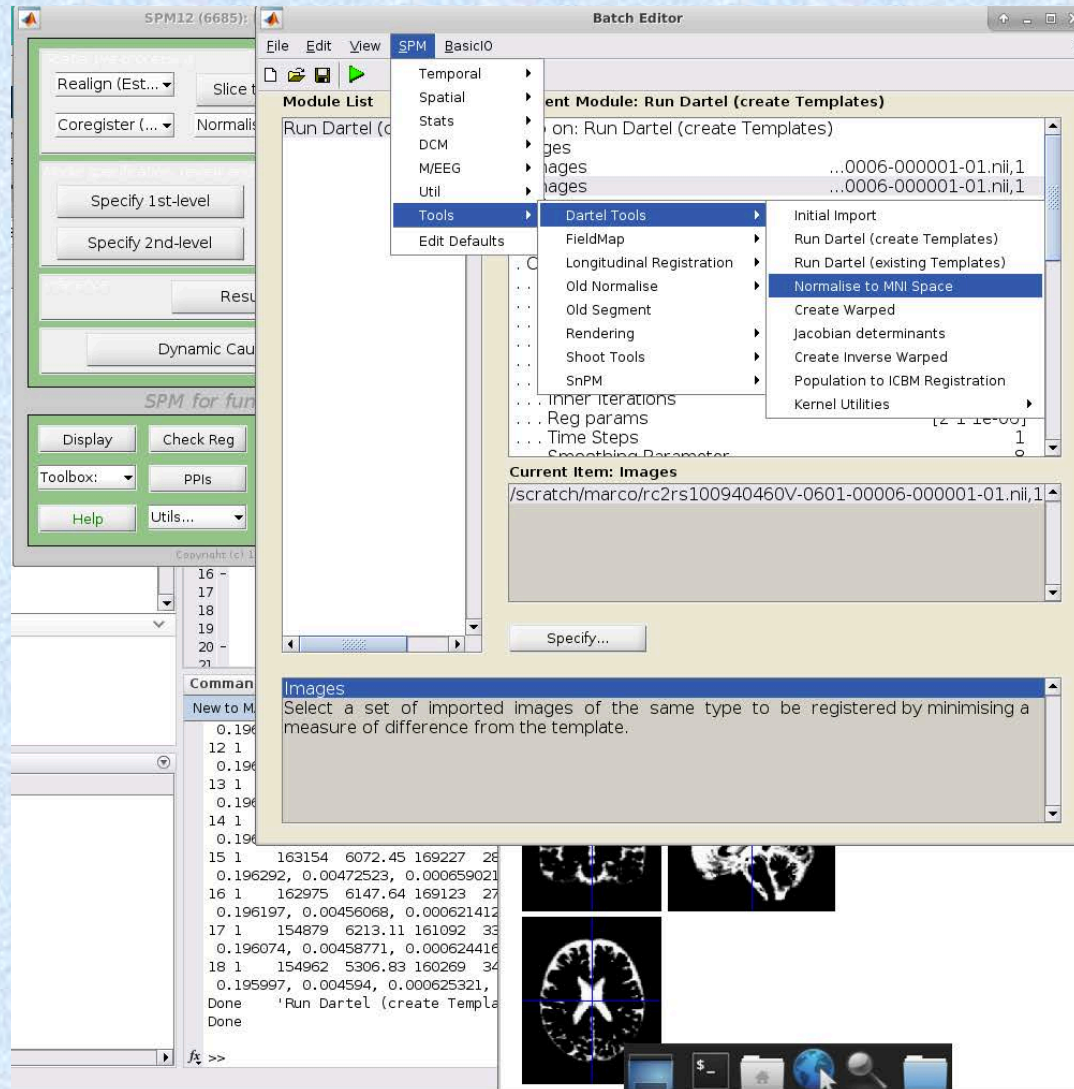


# Select rc1rFilename as first image

# Select rc2rFilename as second image



# 4. Normalise to MNI space



# Select Few Subjects, Add Subject

## Select u\_rc1rFilename as Flow field

## Select c1rFilename as image

The image shows two side-by-side screenshots of a software interface. Both panels are titled 'Current Module: Normalise to MNI Space'. The left panel shows a list of options with 'Flow Field' selected. The right panel shows the same list with 'Images' selected. Below each list is a text field for the 'Current Item' and a 'Specify...' button. At the bottom left, a status bar shows 'Flow Field' and 'Dartel flow field for this subject.'

**Module List**

Normalise to MNI Spa

**Current Module: Normalise to MNI Space**

Help on: Normalise to MNI Space  
Dartel Template /scratch/marco/Template 6.nii  
Select according to  
 . Few Subjects  
 . . Subject  
 . . . Flow Field ...06-000001-01\_Template.nii  
 . . . Images <-X  
Voxel sizes [NaN NaN NaN]  
Bounding box 2x3 double  
Preserve Preserve Concentrations  
Gaussian FWHM [8 8 8]

**Current Item: Flow Field**

/scratch/marco/u rc1rs100940460V-0601-00006-000001-01 T

Specify...

**Current Module: Normalise to MNI Space**

Help on: Normalise to MNI Space  
Dartel Template /scratch/marco/Template 6.nii  
Select according to  
 . Few Subjects  
 . . Subject  
 . . . Flow Field ...06-000001-01\_Template.nii  
 . . . Images ...-0601-00006-000001-01.nii  
Voxel sizes [NaN NaN NaN]  
Bounding box 2x3 double  
Preserve Preserve Concentrations  
Gaussian FWHM [8 8 8]

**Current Item: Images**

/scratch/marco/c1rs100940460V-0601-00006-000001-01.nii

Specify...

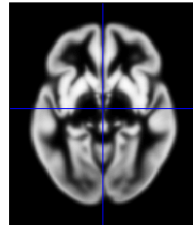
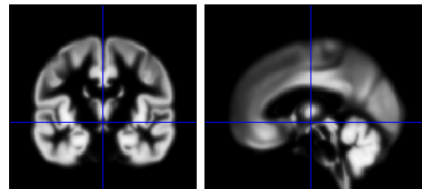
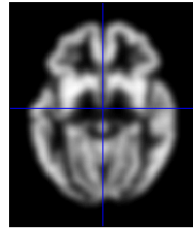
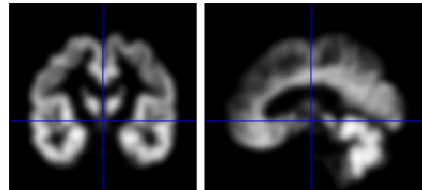
**Flow Field**  
Dartel flow field for this subject.



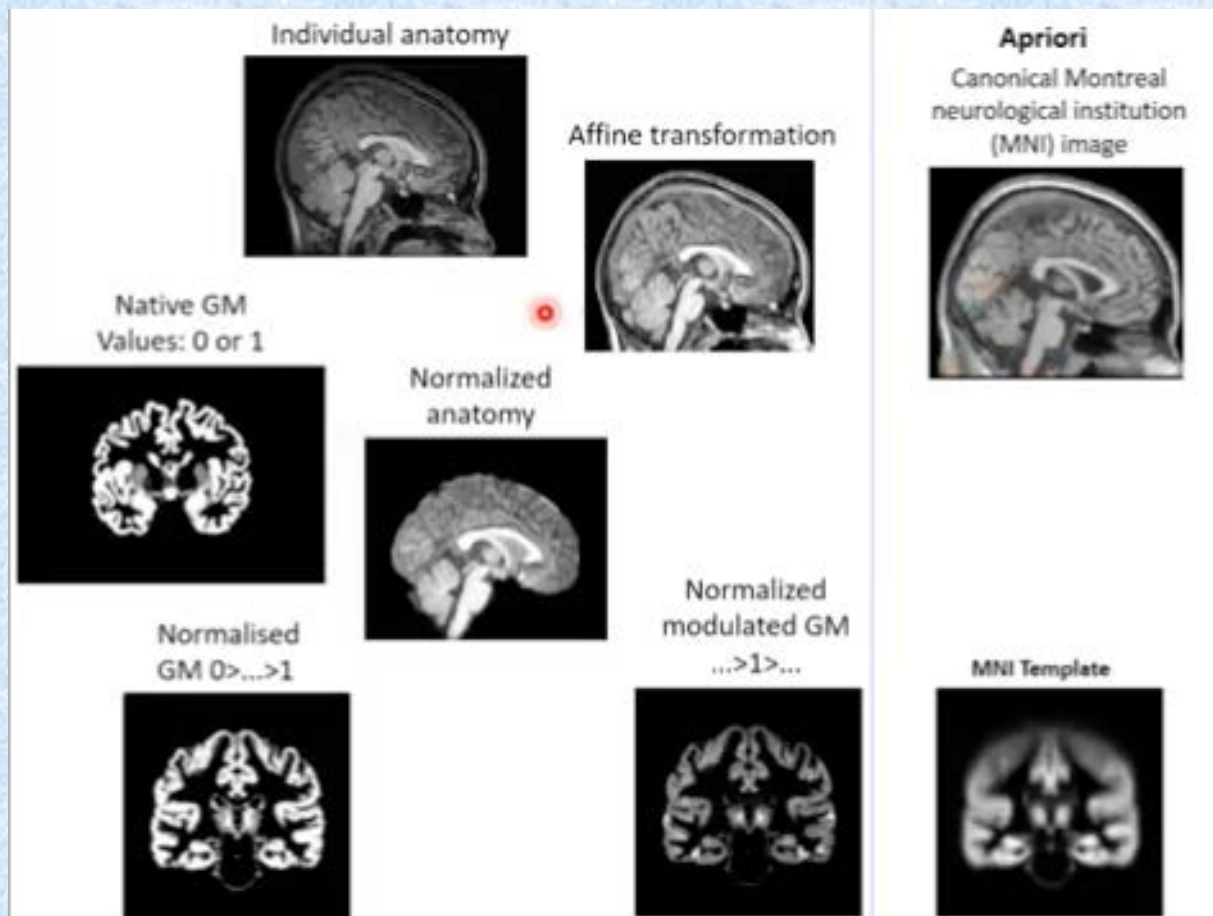
# Finally the result (Check Reg)

Selected 2/[1-24] files. (Added 1/1 file.)

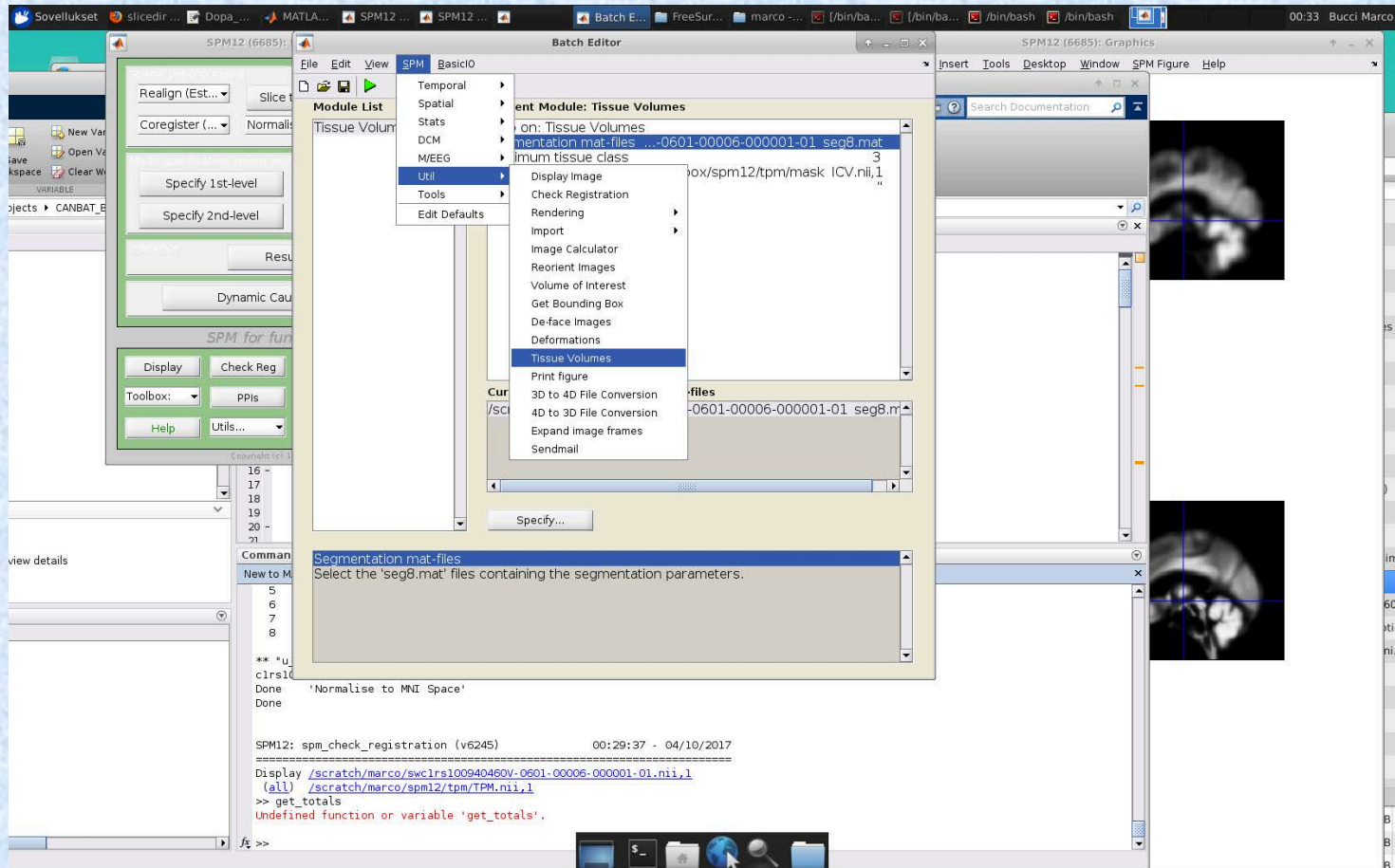
/scratch/marco/swc1rs100940460V-0601-00006-000001-01.nii,1  
/scratch/marco/spm12/tpm/TPM.nii,1



# Summary VBM process

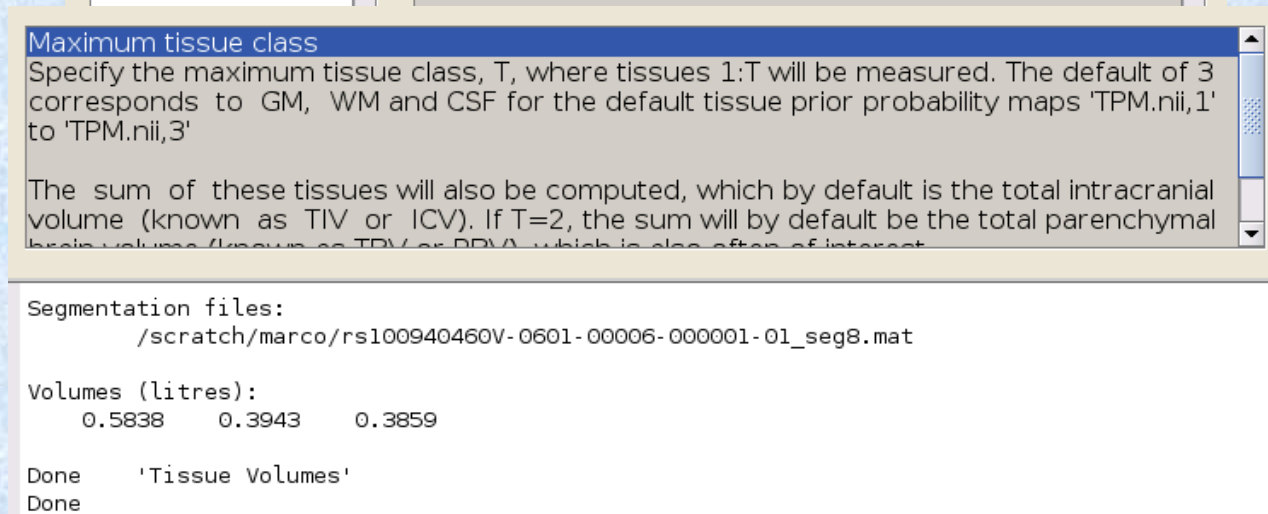
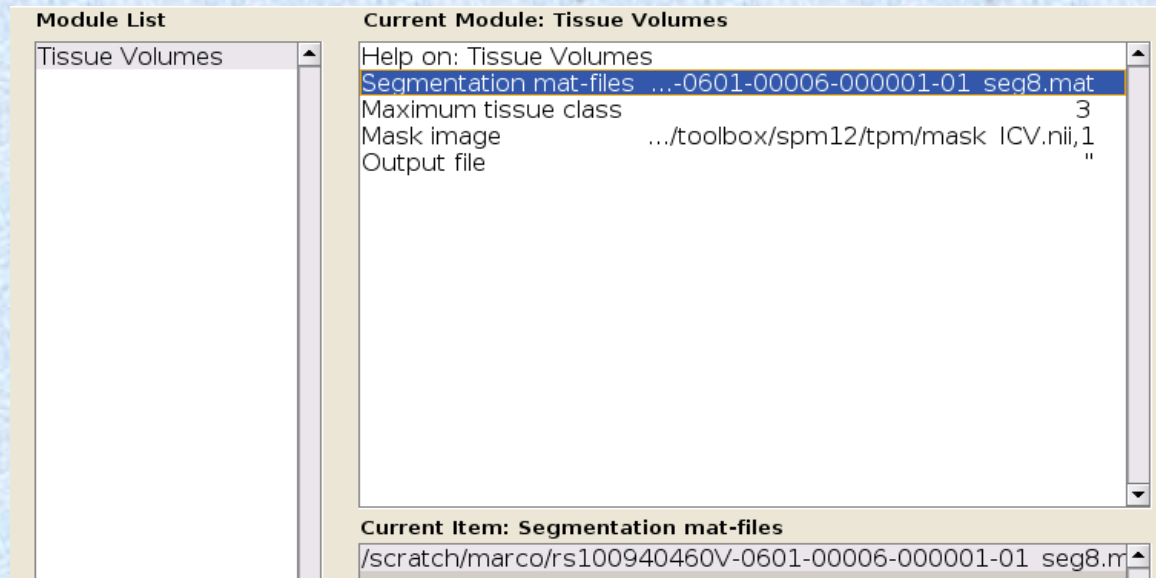


# 5. Stats – Calculation of TIV (total intracranial volume)

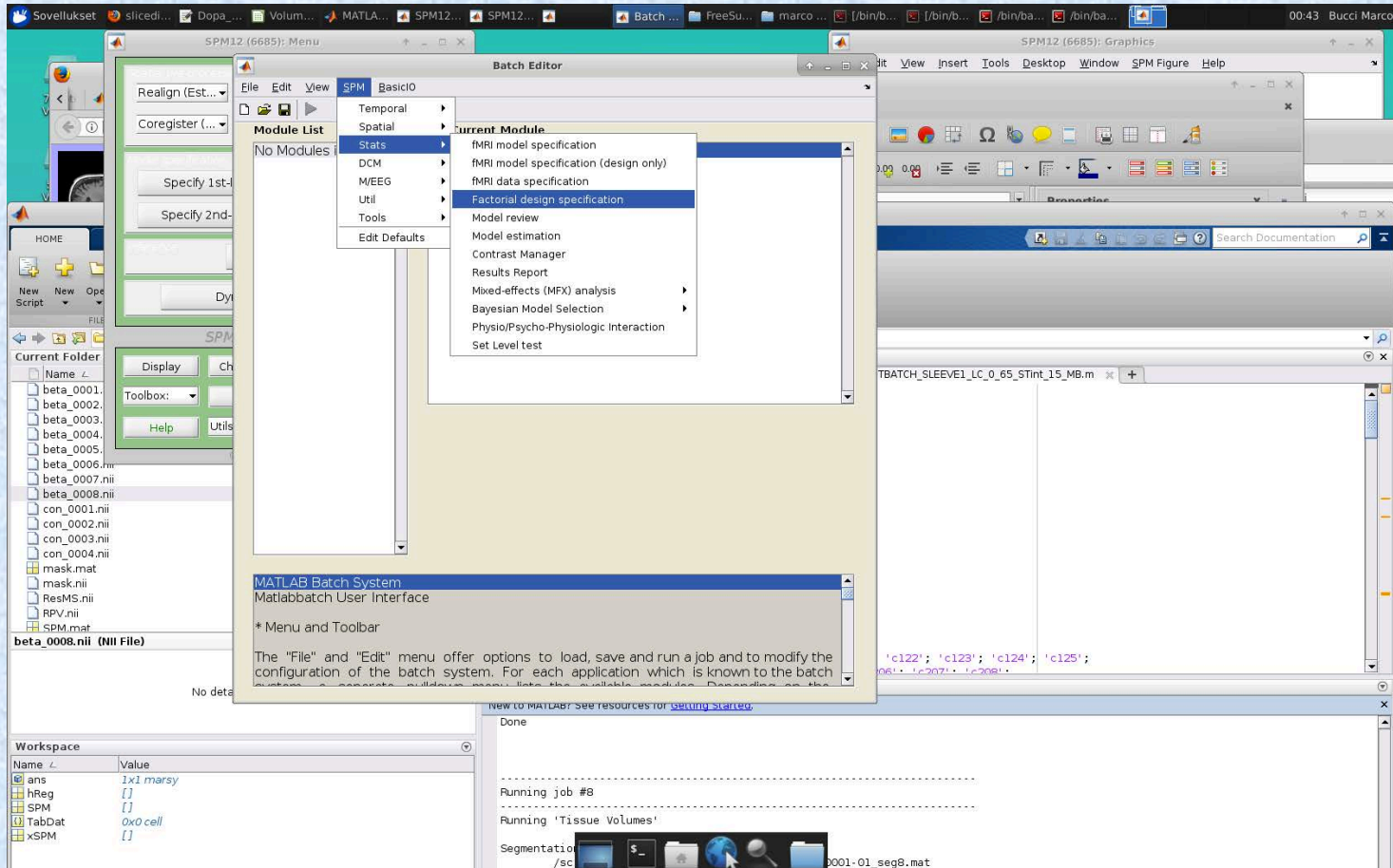




Select ...\_seg8.mat as Segm. file  
Results are shown in Matlab command window unless the output file is specified



# 6. SPM analysis (just a teaser)



# Use of covariates with VBM images. The importance of TIV.

The screenshot displays a software interface with two main panels. The left panel, titled 'Module List', contains a single entry: 'Factorial design speci'. The right panel, titled 'Current Module: Factorial design specification', shows a hierarchical tree of options. The 'Covariates' section is expanded, and the 'Vector' option is selected, highlighted in blue. To the right of the 'Vector' option, the value '65' is displayed. Below the tree view, the 'Current Item: Vector' field contains the value '65'. A 'Specify...' button is located at the bottom of the right panel.

Module	Sub-module	Value
Factorial design specification	Help on: Factorial design specification	
	Directory	<-X
	Design	
	. One-sample t-test	
	. . Scans	<-X
	Covariates	
	. Covariate	
	. . Vector	[1 35]
	. . Name	TIV
	. . Interactions	None
	. . Centering	Overall mean
	. Covariate	
	. . Vector	65
	. . Name	Age
	. . Interactions	None
	. . Centering	Overall mean
	Multiple covariates	
	Masking	

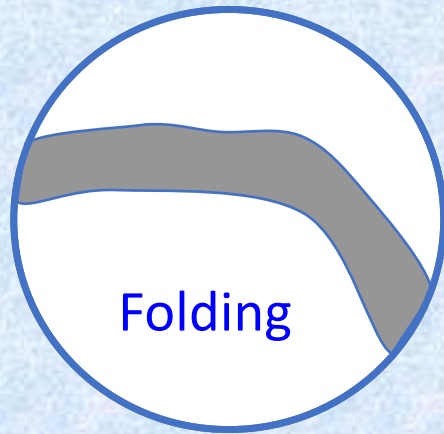
Current Item: Vector

65

Specify...



# Some Explanations of the Differences



# Reference for VBM Dartel

Volodymyr B. Bogdanov

<https://www.youtube.com/watch?v=YVDG9cjn>  
UPU (50 min only on DARTEL VBM)

- Info on scripting the batch files for multiple studies

# Freesurfer analysis



# Freesurfer in a nutshell

- Neuroimaging analysis software package (Open Source)
- Detailed characterization of anatomy (Cortex thickness, folding patterns, ROIs, Subcortical - structure boundaries, Hippocampal subfields)
- Longitudinal analysis (detect changes)
- Statistical tools (GLM, LME, ...), group comparison
- Multi modal integration:

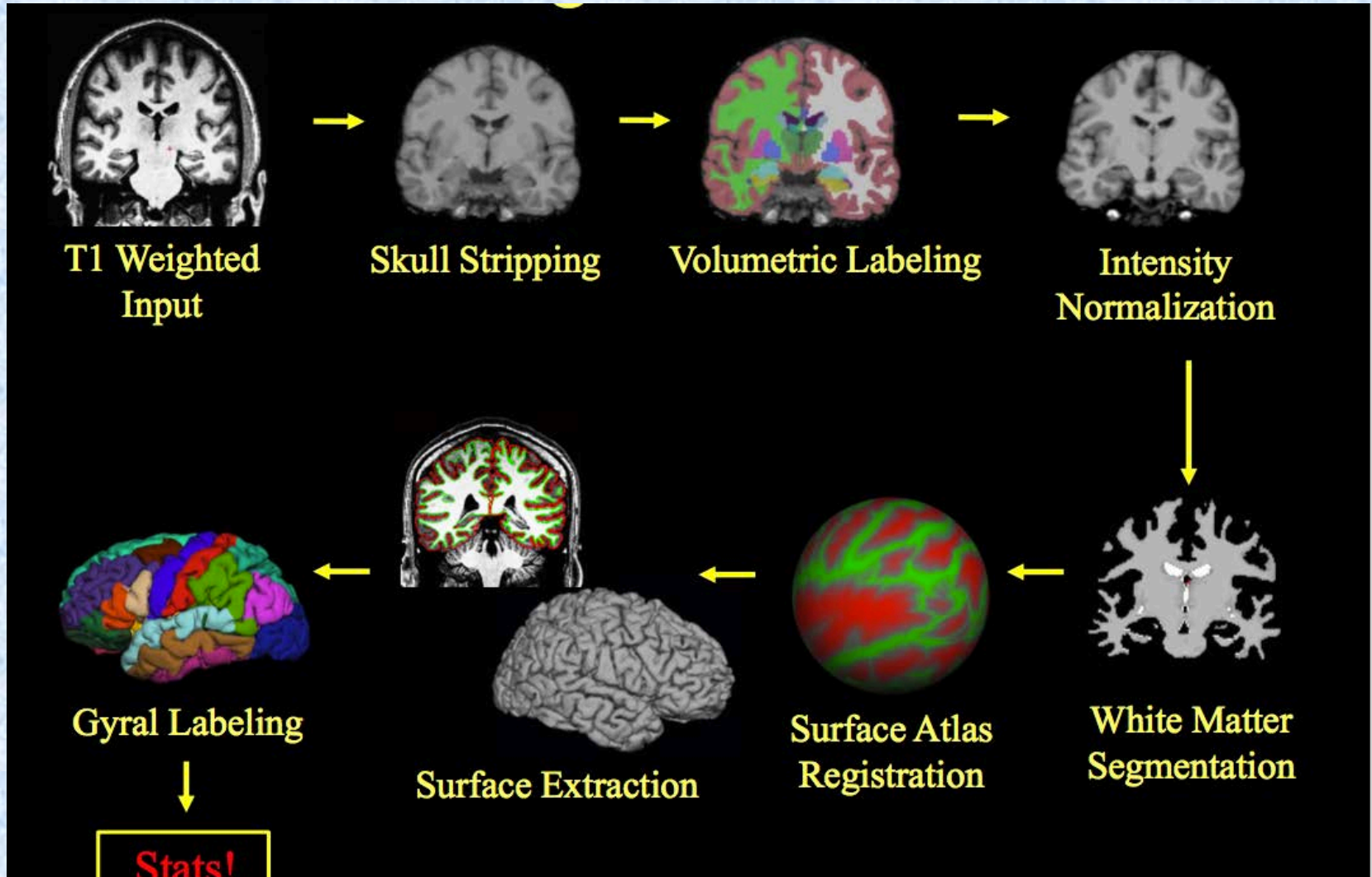
MRI

fMRI (task, rest)

DWI Tractography

PET

# Freesurfer pipeline outline



Simpler than SPM and fully automated... One command:

recon-all -i file.dcm -subject karl -all

Results will be stored in  
\$SUBJECTS\_DIR/karl

The default directory should be set when  
installing the software:

setenv SUBJECTS\_DIR /specificpath/

Slower than SPM, one subject might take up to 20  
hours of processing



# Freesurfer terminology

ROI = Region Of Interest

Volume/Image (Subcortical):

- Segmentation
  - (subcortical automatic segmentation = aseg)

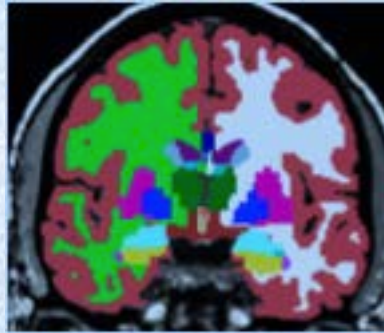
Surface (Cortical):

- Parcellation/Annotation
  - (subcortical automatic segmentation = aparc)
- Clusters, Masks, Labels we created



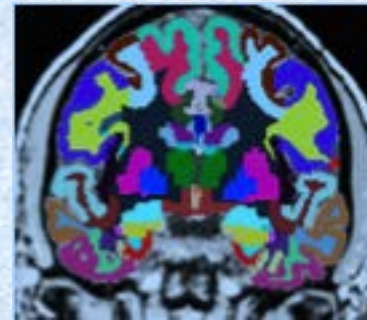
# Segmentation

- Output:



- Volumes

- (for surfaces) Surface segmentation



- Volume-style format (mgz, nii, nii.gz)

- Each voxel has one index (number ID)

- Index List can be found in color lookup table (LUT):  
\$FREESURFER\_HOME/FreeSurferColorLUT.txt

- aseg.mgz, aparc+aseg.mgz, wmparc.mgz

# Slower than SPM, one subject might take up to 20 hours of processing

- Freesurfer outputs in karl/stats the results of the segmentation, volumes and thicknesses:

```
aseg.stats – subcortical volumetric stats
wmparc.stats – white matter segmentation volumetric stats
lh.aparc.stats – left hemi Desikan/Killiany surface stats
rh.aparc.stats – right hemi Desikan/Killiany surface stats
lh.aparc.a2009.stats – left hemi Destrieux
rh.aparc.a2009.stats – right hemi Destrieux
```

- ROI summary example:

Index	SegId	NVoxels	Volume_mm3	StructName	normMean	normStdDev	normMin	normMax	normRange
1	1	0	0.0	Left-Cerebral-Exterior	0.0000	0.0000	0.0000	0.0000	0.0000
2	2	265295	265295.0	Left-Cerebral-White-Matter	106.6763	8.3842	35.0000	169.0000	134.0000
3	3	251540	251540.0	Left-Cerebral-Cortex	81.8395	10.2448	29.0000	170.0000	141.0000
4	4	7347	7347.0	Left-Lateral-Ventricle	42.5800	12.7435	21.0000	90.0000	69.0000
5	5	431	431.0	Left-Inf-Lat-Vent	66.2805	11.4191	30.0000	95.0000	65.0000
6	6	0	0.0	Left-Cerebellum-Exterior	0.0000	0.0000	0.0000	0.0000	0.0000
....									

- To generate spreadsheets of group data:
  - asegstats2table –help
  - aparcstats2table --help



# Aseg.stats

Index	SegId	NVoxels	Volume_mm3	StructName	Mean	StdDev	Min	Max	Range
1	4	5855	5855.0	Left-Lateral-Ventricle	37.7920	10.9705	20.0000	88.0000	68.0000
2	5	245	245.0	Left-Inf-Lat-Vent	56.4091	9.5906	26.0000	79.0000	53.0000
3	7	16357	16357.0	Left-Cerebellum-White-Matter	91.2850	4.8989	49.0000	106.0000	57.0000
4	8	60367	60367.0	Left-Cerebellum-Cortex	76.3620	9.5724	26.0000	135.0000	109.0000
5	10	7460	7460.0	Left-Thalamus-Proper	91.3778	7.4668	43.0000	108.0000	65.0000
6	11	3133	3133.0	Left-Caudate	78.5801	8.2886	42.0000	107.0000	65.0000
7	12	5521	5521.0	Left-Putamen	86.9680	5.5752	66.0000	106.0000	40.0000
8	13	1816	1816.0	Left-Pallidum	97.7162	3.4302	79.0000	106.0000	27.0000
9	14	852	852.0	3rd-Ventricle	41.9007	11.8230	22.0000	69.0000	47.0000
10	15	1820	1820.0	4th-Ventricle	39.7053	10.6407	20.0000	76.0000	56.0000
11	16	25647	25647.0	Brain-Stem	85.2103	8.2819	38.0000	106.0000	68.0000
12	17	4467	4467.0	Left-Hippocampus	77.6346	7.5845	45.0000	107.0000	62.0000
13	18	1668	1668.0	Left-Amygdala	74.5104	5.8320	50.0000	94.0000	44.0000
14	24	1595	1595.0	CSF	52.1348	11.6113	29.0000	87.0000	58.0000

Index: nth Segmentation in stats file

SegId: index into lookup table

Nvoxel: number of Voxel in segmentation

Volume: Volume

StructName: name of structure from LUT

Mean/Std/Min/Max/Range: intensity across ROI

# Aseg.stats Global Measures: Cortical, Gray, White, Intracranial Volumes

Also in aseg.stats header:

```
# Measure lhCortex, lhCortexVol, Left hemisphere cortical gray matter volume, 192176.447567, mm^3
# Measure rhCortex, rhCortexVol, Right hemisphere cortical gray matter volume, 194153.9526, mm^3
# Measure Cortex, CortexVol, Total cortical gray matter volume, 386330.400185, mm^3
# Measure lhCorticalWhiteMatter, lhCorticalWhiteMatterVol, Left hemisphere cortical white matter volume,
  217372.890625, mm^3
# Measure rhCorticalWhiteMatter, rhCorticalWhiteMatterVol, Right hemisphere cortical white matter volume,
  219048.187500, mm^3
# Measure CorticalWhiteMatter, CorticalWhiteMatterVol, Total cortical white matter volume, 436421.078125, mm^3
# Measure SubCortGray, SubCortGrayVol, Subcortical gray matter volume, 182006.000000, mm^3
# Measure TotalGray, TotalGrayVol, Total gray matter volume, 568336.400185, mm^3
# Measure SupraTentorial, SupraTentorialVol, Supratentorial volume, 939646.861571, mm^3
# Measure IntraCranialVol, ICV, Intracranial Volume, 1495162.656130, mm^3
```

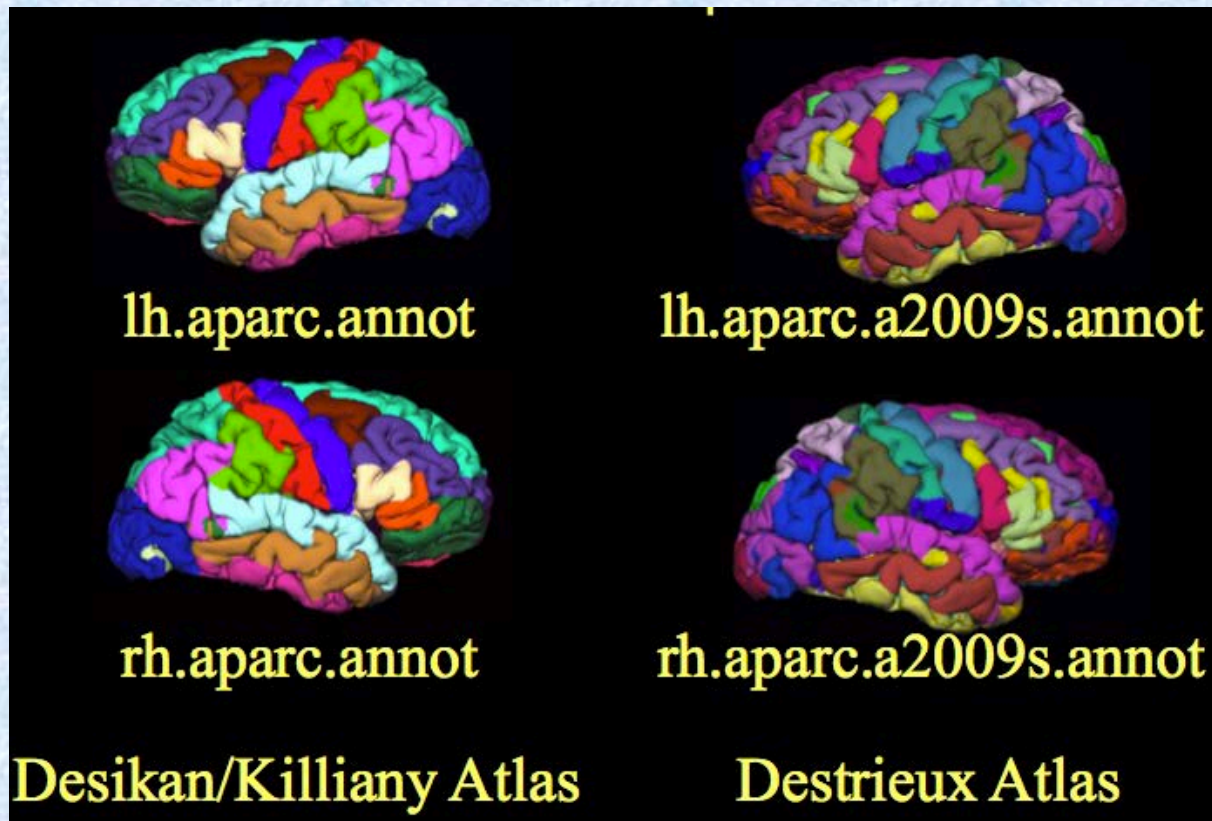
lhCortex, rhCortex, Cortex: surface-based cortical gray matter volume  
lhCorticalWhiteMatter, ... : surface-based cortical white matter volume  
SubCortGray: volume-based  
IntraCranialVol: Estimated Total Intracranial volume (eTIV)

<http://surfer.nmr.mgh.harvard.edu/fswiki/eTIV>



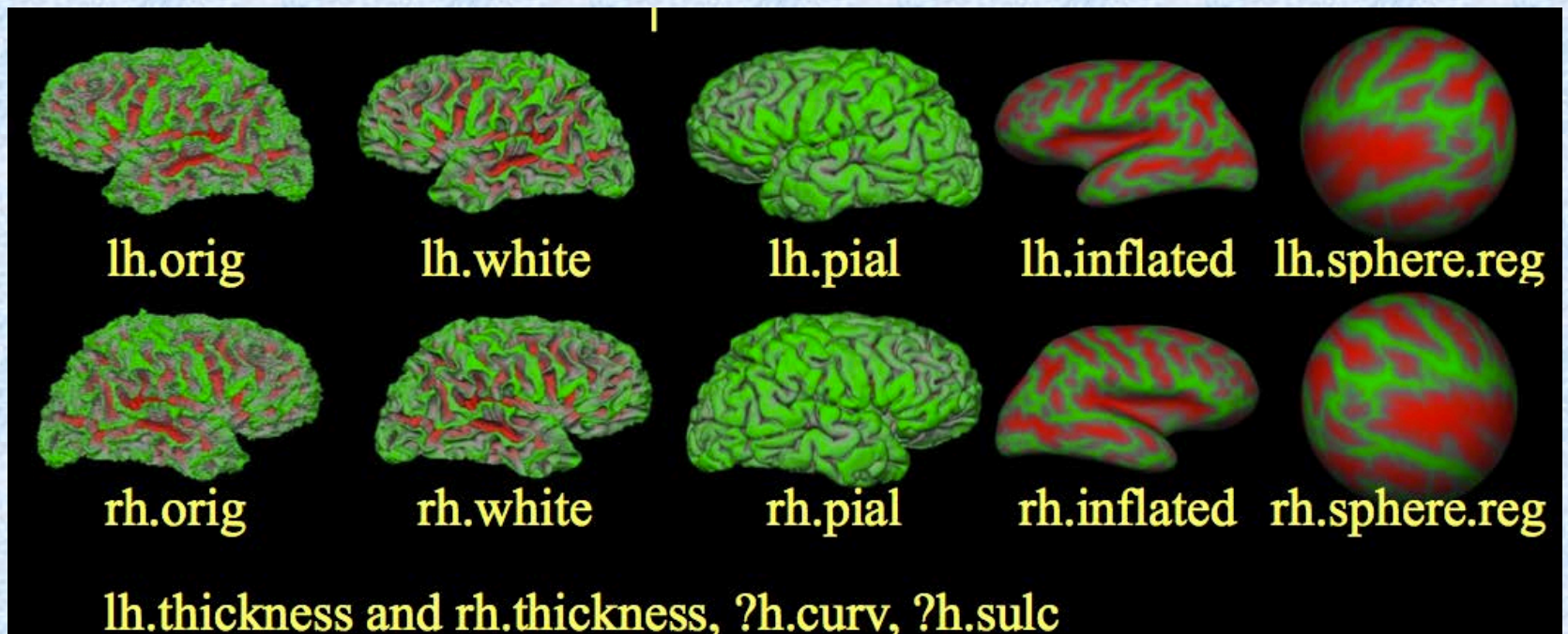
# Freesurfer upon completion, outputs the labels...

- In karl/labels we can find

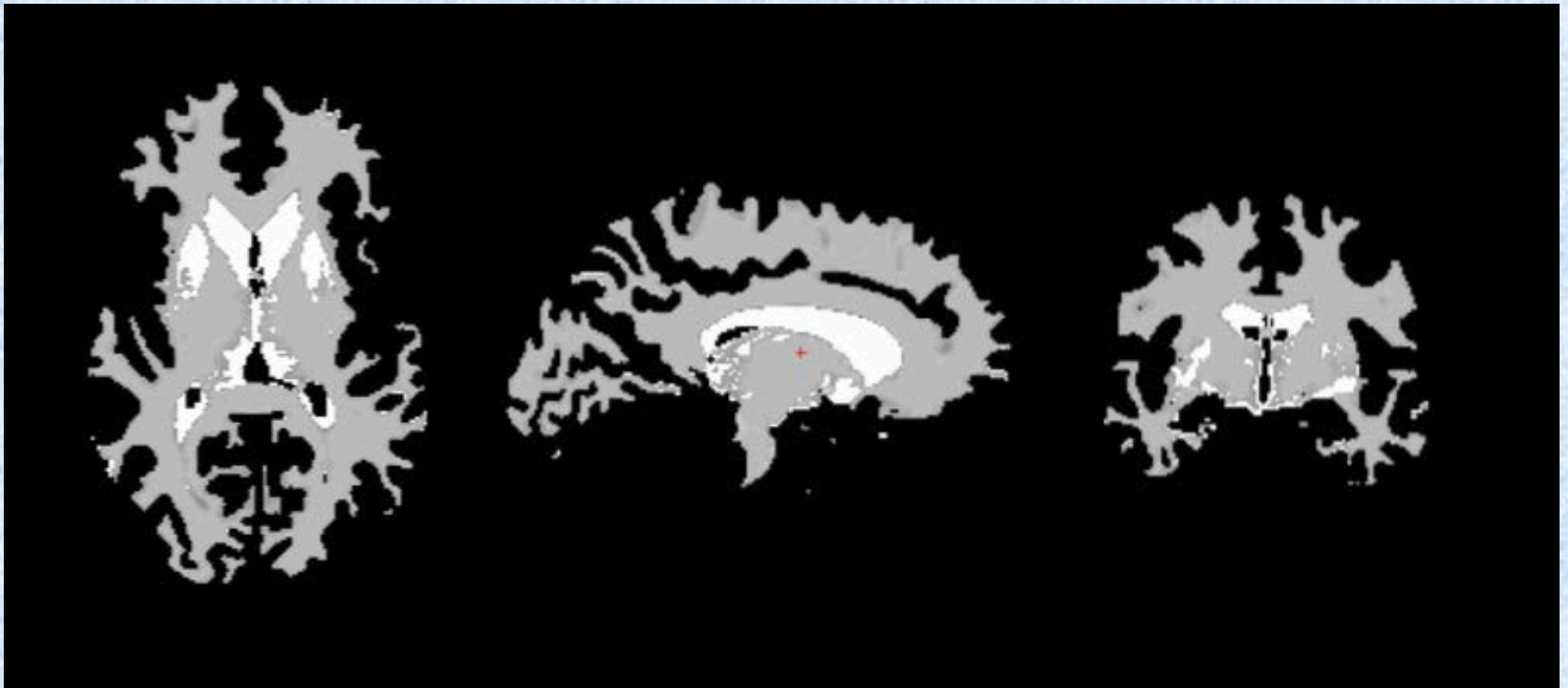


Surfaces are extracted and saved and cortical thickness analysis can be performed on these (SURFSTAT in Matlab, for example)

- In karl/surf we can find



# “White matter” segmentation



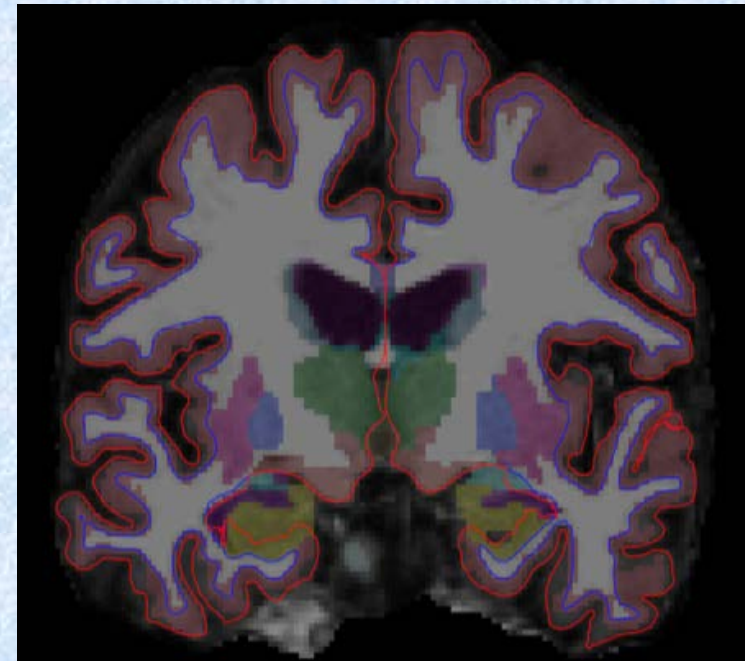
- Brain stem included!
- Cerebellum excluded!
- Not like VBM segmented white matter



# Freeview - Visualisation

```
freeview -v \  
karl/mri/T1.mgz \  
karl/mri/wm.mgz \  
karl/mri/brainmask.mgz \  
karl/mri/aseg.mgz:colormap=lut:opacity=0.2 \  
-f karl/surf/lh.white:edgecolor=blue \  
karl/surf/lh.pial:edgecolor=red \  
karl/surf/rh.white:edgecolor=blue \  
karl/surf/rh.pial:edgecolor=red
```

- -v for volumes,
- -f for surfaces





# Resource for freesurfer

- <http://surfer.nmr.mgh.harvard.edu/fswiki/>
- FreeSurfer Course Copenhagen 2016  
<https://fscph.nru.dk/programme.html>

Thank you

# Import DICOM in SPM

- SPM > Util > Dicom Import

