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 MRI

Preprocessing

Spatially Normalised Grey Matter Image

Group-wise statistics
Voxel-based morphometry – preprocessing overview

Slide from Hobbs & Novak, MfD (2008)
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 (3rd 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
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

[Diagram showing the VBM process with steps including individual anatomy, affine transformation, normalized anatomy, normalized modulated GM, and MNI template.]
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.

Module List
- Tissue Volumes

Current Module: Tissue Volumes
Help on: Tissue Volumes
Segmentation mat-files .../0601-00006-000001-01 seg8.mat
Maximum tissue class 3
Mask image .../toolbox/spm12/tpm/mask ICV.nii,1
Output file

Current Item: Segmentation mat-files
/scratch/marco/rs100940460V-0601-00006-000001-01 seg8.mat

Maximum tissue class
Specify the maximum tissue class, T, where tissues 1:T will be measured. The default of 3 corresponds to GM, WM and CSF for the default tissue prior probability maps 'TPM.nii,1' to 'TPM.nii,3'.

The sum of these tissues will also be computed, which by default is the total intracranial volume (known as TIV or ICV). If T=2, the sum will by default be the total parenchymal tissue volume (known as TIV or PDI), which is also often of interest.

Segmentation files:
/scratch/marco/rs100940460V-0601-00006-000001-01 seg8.mat

Volumes [litres]:
0.5838 0.3943 0.3859

Done 'Tissue Volumes'
Done
6. SPM analysis (just a teaser)
Use of covariates with VBM images. The importance of TIV.
Some Explanations of the Differences

- Folding
- Thickening
- Thinning
- Mis-classify
- Mis-register
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

1. T1 Weighted Input
2. Skull Stripping
3. Volumetric Labeling
4. Intensity Normalization
5. Gyral Labeling
6. Surface Extraction
7. Surface Atlas Registration
8. White Matter Segmentation

Stats!
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 = \texttt{aseg})

Surface (Cortical):

• Parcellation/Annotation
  • (subcortical automatic segmentation = \texttt{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
  - `wm parc.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:

<table>
<thead>
<tr>
<th>Index</th>
<th>SegId</th>
<th>N Voxels</th>
<th>Volume mm³</th>
<th>StructName</th>
<th>normMean</th>
<th>normStdDev</th>
<th>normMin</th>
<th>normMax</th>
<th>normRange</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0.0</td>
<td>Left-Cerebral-Exterior</td>
<td>0.0000</td>
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<tr>
<td>2</td>
<td>2</td>
<td>265295</td>
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<td>Left-Cerebral-White-Matter</td>
<td>106.6763</td>
<td>8.3842</td>
<td>35.0000</td>
<td>169.0000</td>
<td>134.0000</td>
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<td>3</td>
<td>251540</td>
<td>251540.0</td>
<td>Left-Cerebral-Cortex</td>
<td>81.8395</td>
<td>10.2448</td>
<td>29.0000</td>
<td>170.0000</td>
<td>141.0000</td>
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<tr>
<td>4</td>
<td>4</td>
<td>7347</td>
<td>7347.0</td>
<td>Left-Lateral-Ventricle</td>
<td>42.5800</td>
<td>12.7435</td>
<td>21.0000</td>
<td>90.0000</td>
<td>69.0000</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>431</td>
<td>431.0</td>
<td>Left-Inf-Lat-Vent</td>
<td>66.2805</td>
<td>11.4191</td>
<td>30.0000</td>
<td>95.0000</td>
<td>65.0000</td>
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<td>0.0000</td>
<td>0.0000</td>
<td>0.0000</td>
<td>0.0000</td>
</tr>
</tbody>
</table>

- To generate spreadsheets of group data:
  - `asegstats2table --help`
  - `aparcstats2table --help`
### Aseg.stats

<table>
<thead>
<tr>
<th>Index</th>
<th>SegId</th>
<th>Nvoxels</th>
<th>Volume_mm³</th>
<th>StructName</th>
<th>Mean</th>
<th>StdDev</th>
<th>Min</th>
<th>Max</th>
<th>Range</th>
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</thead>
<tbody>
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<td>245.0</td>
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<td>9.5906</td>
<td>26.0000</td>
<td>79.0000</td>
<td>53.0000</td>
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<td>Left-Cerebellum-White-Matter</td>
<td>91.2850</td>
<td>4.8989</td>
<td>49.0000</td>
<td>106.0000</td>
<td>57.0000</td>
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<td>9.5724</td>
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<td>135.0000</td>
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<td>Left-Pallidum</td>
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<td>3.4302</td>
<td>79.0000</td>
<td>106.0000</td>
<td>27.0000</td>
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<tr>
<td>9</td>
<td>14</td>
<td>852</td>
<td>852.0</td>
<td>3rd-Ventricle</td>
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<td>47.0000</td>
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<td>1820</td>
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<td>4th-Ventricle</td>
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<td>10.6407</td>
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<td>76.0000</td>
<td>56.0000</td>
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<tr>
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<td>16</td>
<td>25647</td>
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<td>Brain-Stem</td>
<td>85.2103</td>
<td>8.2819</td>
<td>38.0000</td>
<td>106.0000</td>
<td>68.0000</td>
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<tr>
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<td>Left-Hippocampus</td>
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<td>11.6113</td>
<td>29.0000</td>
<td>87.0000</td>
<td>58.0000</td>
</tr>
</tbody>
</table>

- **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, mm³
- Measure rhCortex, rhCortexVol, Right hemisphere cortical gray matter volume, 194153.9526, mm³
- Measure Cortex, CortexVol, Total cortical gray matter volume, 386330.400185, mm³
- Measure lhCorticalWhiteMatter, lhCorticalWhiteMatterVol, Left hemisphere cortical white matter volume, 217372.890625, mm³
- Measure rhCorticalWhiteMatter, rhCorticalWhiteMatterVol, Right hemisphere cortical white matter volume, 219048.187500, mm³
- Measure CorticalWhiteMatter, CorticalWhiteMatterVol, Total cortical white matter volume, 436421.078125, mm³
- Measure SubCortGray, SubCortGrayVol, Subcortical gray matter volume, 182006.000000, mm³
- Measure TotalGray, TotalGrayVol, Total gray matter volume, 568336.400185, mm³
- Measure SupraTentorial, SupraTentorialVol, Supratentorial volume, 939646.861571, mm³
- Measure IntraCranialVol, ICV, Intracranial Volume, 1495162.656130, mm³

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:

  - lh.aparc.annot
  - lh.aparc.a2009s.annot
  - rh.aparc.annot
  - rh.aparc.a2009s.annot

Desikan/Killiany Atlas  Destrieux Atlas
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

lh.orig  lh.white  lh.pial  lh.inflated  lh.sphere.reg
rh.orig  rh.white  rh.pial  rh.inflated  rh.sphere.reg

lh.thickness and rh.thickness, lh.curv, lh.sulc
“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

[Image of a software interface showing the import of DICOM files into SPM.]