SPM course 2012 Lausanne

Computational Anatomy

Laboratoire de Recherche en Neuro-Imagerie
Motivation

- Genetic predisposition
- Neural signature
- Synaptic plasticity
- Training
- Lesion
- Behaviour
Methods

**surface**

- Fischl et al., 1999 *Neuroimage*
- Cykowski et al., 2008 *Cereb Cortex*

**shape**

- Ashburner & Friston, 2000 *Neuroimage*
- Jones et al., 2005 *Neuroimage*
- Hutton et al., 2009 *Neuroimage*

**voxel-based**
Prerequisites

• Anatomical scans can also help us infer brain function.
  – Do people with chronic depression show brain atrophy?
  – Which brain regions atrophy with age?
  – Do people with good spatial memory (taxi drivers) have different anatomy than other people?

• Voxel-based morphometry is a tool to relate grey matter volume with medical history and behaviour
• Cross-sectional studies

  – Can compare two distinct populations

  – Can also examine atrophy through time, though will require more people than longitudinal VBM.

• Longitudinal VBM

  – Sensitive way to detect atrophy through time. Using the same individual reduces variability.

• VBM findings are first step in understanding structural changes.
Morphometry examines the shape, volume and integrity of structures.

Classically, morphometry was conducted by manually segmenting a few regions of interest.

Voxel based morphometry conducts an independent statistical comparison for each voxel in the brain.
VBM has some advantages over manual tracing:

- Automated: fast and not subject to individual bias.

- Able to examine regions that are not anatomically well defined.

- Able to see the whole brain

- Normalisation compensates for overall differences in brain volume, which can add variance to manual tracing of un-normalised images.
Scan Volume: Field of View (FOV), e.g. 192 mm

Matrix Size e.g., 192 x 192
In-plane resolution
192 mm / 192
= 1 mm

Slice thickness e.g., 1 mm

Voxel Size (volumetric pixel)
examples
We can statistically analyze gray matter atrophy
Neurodegenerative diseases

• Alzheimer’s disease
  – 6 different MR scanner
  – Major software updates
  – 10 years of data acquisition

• Chorea Huntington
  – Pre-symptomatic stage

Stonnington et al., 2008 *Neuroimage*
Thieben et al., 2002 *Brain*
Higher cognitive functions

Fig. 3 Gray-matter volume correlated with introspective ability. (A) Projection of statistical (T) maps for positive (hot color map: red, orange, yellow) and negative (cool color map: blue) correlations with $A_{10c}$ onto an inflated cortical surface (T1-weighted template, thresholded at $T > 3$ for display purposes). Significant clusters ($P < 0.05$, corrected for multiple comparisons) where metacognitive ability correlated with gray-matter volume (see SOM methods) were found in right anterior PFC (BA 10, positive correlation) and the left inferior temporal gyrus (negative correlation), accompanied by contralateral homologous clusters at $P < 0.001$, uncorrected. (B) Plot of gray-matter volume in the right BA 10 cluster against both $A_{10c}$ and $d'$ (see SOM methods for full details), indicating that the correlation with metacognitive ability was independent of task performance. a.u., arbitrary units.
Univariate goes multivariate

Stonnington et al., 2008 *Neuroimage*
Klöppel et al., 2007 *Brain*
Brain plasticity
• Taxi drivers – London

• Training = „the Knowledge“

• Posterior HC volume increase

• Positive correlation with navigation experience

Maguire et al. 2000 *PNAS*
Woollett et al., 2009 *PTRSB*
Mode d’emploi
Wellcome Trust Centre for Neuroimaging

http://www.fil.ion.ucl.ac.uk/spm/

https://www.jiscmail.ac.uk/
Data processing

- Original
- Normalized
- GM Segment
- Modulated GM
- Smoothed GM

**Processes:**
- Normalization
- Segmentation
- Modulation
- Smoothing

**Inputs:**
- Template
- GM prior
- WM prior
- CSF prior

**Output:**
- Gaussian Kernel
VBM preprocessing

• Unified Segmentation
  – New Segment
  – Smooth

• DARTEL (alternative)
  – New Segment
  – Create Template
  – Normalise to MNI
• High-resolution MRI reveals fine structural detail in the brain, but not all of it reliable or interesting

  – Noise, intensity-inhomogeneities, vasculature, …

• MR Intensity is usually not quantitatively meaningful (in the same way that e.g. CT is)

• Regional volumes of the three main tissue types: gray matter, white matter and CSF, are well-defined and potentially very interesting
• Uses information from tissue probability maps (TPMs) and the intensities of voxels in the image to work out the probability of a voxel being GM, WM or CSF

**ICBM Tissue Probabilistic Atlases.** These tissue probability maps are kindly provided by the International Consortium for Brain Mapping, John C. Mazziotta and Arthur W. Toga.
• VBM segments image into three tissue types: grey matter, white matter and CSF.
  
  – Typically done on T1 scans (best spatial resolution, good grey-white contrast).
  
  – Only three tissue types: will not cope with large lesions.
  
  – Probability map: each voxel has a 0..100% chance of being one of the 3 tissue types.
Intensities are modelled by a Gaussian Mixture Model (aka Mixture Of Gaussians)

With a specified number of components

Parameterised by means, variances and mixing proportions (prior probabilities for components)

Multiple MoG components per tissue class allow non-Gaussian distributions to be modelled

- E.g. accounting for partial volume effects
- Or possibility of deep GM differing from cortical GM
Segmentation clean-up

$T_1$

masked

mask
Inhomogeneity correction

- MR Images are corrupted by smoothly varying intensity inhomogeneity caused by magnetic field imperfections and subject-field interactions
  - Would make intensity distribution spatially variable
- A smooth intensity correction can be modelled by a linear combination of DCT basis functions
Inhomogeneity correction

- Field inhomogeneity will disrupt intensity based segmentation
- Bias correction required

**no correction**

<table>
<thead>
<tr>
<th></th>
<th>Estimate</th>
<th>T₁</th>
<th>GM</th>
<th>WM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><img src="image1.png" alt="Brain" /></td>
<td><img src="image2.png" alt="Brain" /></td>
<td><img src="image3.png" alt="Brain" /></td>
<td><img src="image4.png" alt="Brain" /></td>
</tr>
</tbody>
</table>
The generative model

• Keeps doing these steps iteratively until the objective function is minimised

• Results in images that are segmented, bias-corrected, and registered into standard space
Summary of the unified model

- SPM5/SPM8 implements a **generative model**
  - Principled Bayesian probabilistic formulation

- Combines deformable tissue probability maps with Gaussian mixture model segmentation
  - The inverse of the transformation that aligns the TPMs can be used to normalise the original image

- Bias correction is included within the model
**VBM preprocessing**

**New Segment**

- Select: Batch → SPM → Tools → New Segment

- Volumes to Segment (Data:Channel:Volumes) – select structural MRI scans

**Optional:** for DARTEL pre-processing select Tissues:Tissue{1}:Native Tissue: Native+DARTEL Imported

- To obtain spatially normalized modulated (preserve amount of signal) images select option: Tissues:Tissue{1}:Warped Tissue: **Modulated**
New segmentation

• An extended work-in-progress algorithm

• Multi-spectral \( \mu_k \rightarrow \mu_k, \sigma_k \rightarrow \sigma_k, \rho \rightarrow \{\rho_s\} \)

• New TPMs including different tissues
  – Reduces problems in non-brain tissue

• New more flexible warping of TPMs
  – More precise and more “sharp/contrasty” results
New segmentation – tissue probability maps

Segment button

New Seg Toolbox
• The tissue probability maps (which are in standard space) are warped to match the image
  – this gives parameters for registering the image into standard space later
Diffeomorphic registration

• VBM is crucially dependent on registration performance
  – The limited flexibility of DCT normalisation has been criticised
  – Inverse transformations are useful, but not always well-defined
  – More flexible registration requires careful modelling and regularisation (prior belief about reasonable warping)
  – MNI/ICBM templates/priors are not universally representative

• The DARTEL toolbox combines several methodological advances to address these limitations

Ashburner (2007) NeuroImage 38:95-113
• Recent papers comparing different approaches have favoured more flexible methods

• DARTEL usually outperforms DCT normalisation
  – Also comparable to the best algorithms from other software packages (though note that DARTEL and others have many tunable parameters...)

• Klein et al. (2009) is a particularly thorough comparison, using expert segmentations
  – Results summarised in the next slide
Klein et al., 2009 *Neuroimage*
Simultaneous registration of GM to GM and WM to WM, for a group of subjects
Unified segmentation
Limitations

- Assumes that the brain consists of only the tissues modelled by the TPMs
  - No allowance for lesions (stroke, tumours, etc)
- Prior probability model is based on relatively young and healthy brains
  - Less appropriate for subjects outside this population
- Needs reasonable quality images to work with
  - No severe artefacts
  - Good separation of intensities
  - Good initial alignment with TPMs...
• **Whether to modulate**

• **How much to smooth**

• **Interpreting results**

• **Adjusting for total GM or Intracranial Volume**

• **Limitations of linear correlation**

• **Statistical validity**
• If someone has atrophy, normalization will stretch grey matter to make brain match healthy template

• This will reduce ability to detect differences
Analogy: as we blow up a balloon, the surface becomes thinner.

Likewise, as we expand a brain area it’s volume is reduced.
• Multiplication of the warped (normalised) tissue intensities so that their regional or global volume is preserved
  
  – Can detect differences in completely registered areas

• Otherwise, we preserve concentrations, and are detecting mesoscopic effects that remain after approximate registration has removed the macroscopic effects
  
  – Flexible (not necessarily “perfect”) registration may not leave any such differences
VBM subtleties

• Whether to modulate

• **How much to smooth**

• Interpreting results

• Adjusting for total GM or Intracranial Volume

• Limitations of linear correlation

• Statistical validity
Smooth

- To get smoothed images select: SPM → Spatial → Smooth
- Click on “Images to Smooth” → Select “Dependency” (bottom right) → Select “New Segment: mwc1 Images”
- Click on “Run batch” (green button)
Smoothing

- Smoothing kernel - should match the shape and size of the expected effect

- Benefits
  - more “Gaussian distribution” of the data
  - Smooth out incorrect registration

- RFT requires FWHM > 3 voxels
• Between 7 and 14mm is probably best
  – (lower is okay with better registration, e.g. DARTEL)
• The analysis will be most sensitive to effects that match the shape and size of the kernel

• The data will be more Gaussian and closer to a continuous random field for larger kernels

• Results will be rough and noise-like if too little smoothing is used

• Too much will lead to distributed, indistinct blobs
VBM subtleties

- Whether to modulate
- How much to smooth
- **Interpreting results**
- Adjusting for total GM or Intracranial Volume
- Limitations of linear correlation
- Statistical validity
Interpretation

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

- Thickening
- Thinning
- Mis-classify
- Mis-register
• Microstructural changes could cause intensity changes
  – T1-weighted imaging not quantitative (cf. T1-quant, MT, etc.)
  – Still potential explanation of findings (or lack thereof)
• Complicated phenomenon…
  – Increased T1w intensity in cortex =>
    • Lower GM prob, prob shifted to WM class
    • Higher GM prob, prob taken from CSF class
• Significant differences still generally interpretable
• Whether to modulate
• How much to smooth
• Interpreting results

• Adjusting for total GM or Intracranial Volume
  • Limitations of linear correlation
  • Statistical validity
Global normalisation

- Total intracranial volume integrates GM, WM and CSF, or attempts to measure the skull-volume directly
  - Not sensitive to global reduction of GM+WM (cancelled out by CSF expansion – skull is fixed!)

- Correcting for TIV in VBM statistics may give more powerful and/or more interpretable results
  - See also
    http://dx.doi.org/10.1016/j.neuroimage.2010.06.025
• **Generic issue** in neuroimaging
  
  – to ensure that the analysis identifies regionally specific “non-global” effects

• Changes in dimension or shape as a function of size
  
  – “global” model
  
  – “mosaic” model

Figure from: *Adjustment for Whole Brain...*  
O’Brian et al, 2006
Shape is really a multivariate concept
- Dependencies among volumes in different regions

SPM is mass univariate
- Combining voxel-wise information with “global” integrated tissue volume provides a compromise

Above: (ii) is globally thicker, but locally thinner than (i) – either of these effects may be of interest to us.

Below: The two “cortices” on the right both have equal volume...

Figures from: Voxel-based morphometry of the human brain… Mechelli et al, 2005
VBM uses the machinery of SPM to localise patterns in regional volumetric variation

The procedure involves

– Unified tissue segmentation (Gaussian mixture modelling with bias correction and spatially registered priors)
– Spatial normalisation using Dartel, with preservation of volume
– Smoothing
– SPM analysis
  • Typically with covariates for age, gender, perhaps TIV and/or total GM

Interpretation is challenging, and caution is advised
– But Science papers and BBC News articles await!
References


Rigid average (Template_0)

Template 1

Template 6
• Automated detection
  – SPM8 „unified segmentation“
  – Fuzzy clustering

• Analysis
  – GM volume
  – Binary & probabilistic lesion maps

Seghier et al., 2008 Neuroimage
• Study design

- Motor learning paradigm – 10-digit sequence

- 3 subjects, 9 weeks

- 15 min/d training @ home

Ward et al., *in preparation*