Aging - cognition, brain imaging and genetics

Multimodal MRI recordings, image processing, and data analysis

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1 March 2013
• Multimodal MRI
  = Collection of MRI recordings obtained with different MR measurement techniques from the same subject - in the same imaging session
  • Structural 3D MRI (sMRI)
  • Diffusion tensor imaging (DTI)
  • Functional BOLD MRI (fMRI) in the resting state
    ↑ Blood Oxygen Level Dependent contrast

• Image processing workflows
  • Brain morphometry (FreeSurfer)
  • White matter integrity and fiber tracking (Diffusion Toolkit & TrackVis)
  • Resting state networks (the FCON1000 scripts)

• Longitudinal data analysis
  • Linear mixed models (R: lmer in the lme4 package)
  • Nonlinear mixed effects estimation (MATLAB: nlmefit)

• Data organization
## The multimodal MRI protocol

**Wave1 2005, Wave2 2008/9, Wave3 2011/12**

1.5 T GE Signa Excite MRI scanner with a standard 8 chn receive only head coil:

<table>
<thead>
<tr>
<th>Series</th>
<th>Pulse sequence parameters</th>
<th>W1</th>
<th>W2</th>
<th>W3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Localizer 2D</td>
<td>TR/TE = 7.8[ms]/1.7[ms]/30[°]; acq.voxel: 1.0 × 1.0 × 5.0 [mm³]; 3 [imgs]</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>2 Ax PD/T2 2D FSE</td>
<td>TR/TE₁/TE₂/FA = 3840/12.1/84.9/90; voxel: 0.94 × 0.94 × 4.0; 52</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 Sag T1 3D FSPGR IR preped</td>
<td>TR/TE/TI/FA = 9.45/2.41/450/7; voxel: 0.94 × 0.94 × 1.40; 124</td>
<td></td>
<td>√</td>
<td></td>
</tr>
<tr>
<td>4 Sag T1 3D FSPGR IR preped</td>
<td>[ same as 3 to improve SNR for FreeSurfer segmentation ]</td>
<td></td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>5 Sag T1 3D FSPGR IR preped</td>
<td>TR/TE/TI/FA = 9.12/1.77/450/7; voxel: 0.94 × 0.94 × 1.40; 124</td>
<td></td>
<td>√</td>
<td></td>
</tr>
<tr>
<td>6 Sag T1 3D FSPGR IR preped</td>
<td>[ same as 5 to improve SNR for FreeSurfer segmentation ]</td>
<td></td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>7 Ax DTI, EP SE, 26 slices</td>
<td>TR/TE/FA = 7900/97.1/90; 25 b=1000, 5 b=0; voxel: 0.94 × 0.94 × 4.0; 780</td>
<td></td>
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<td>√</td>
</tr>
<tr>
<td>8 Ax DTI, EP SE, 25 slices</td>
<td>TR/TE/FA = 7900/104.8/90; 25 b=1000, 5 b=0; voxel: 0.94 × 0.94 × 4.0; 750</td>
<td></td>
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<td>√</td>
</tr>
<tr>
<td>9 Ax DTI, EP SE, 25 slices</td>
<td>TR/TE/FA = 7900/110.5/90; 25 b=1000, 5 b=0; voxel: 0.94 × 0.94 × 4.0; 750</td>
<td></td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>10 Ax fMRI GRE EPI Resting</td>
<td>TR/TE/FA=2000/50/90; voxel: 3.75 × 3.75 × 5.5; 25 slices; 256 volumes; 6400</td>
<td></td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>11 Ax fMRI GRE EPI Fingertap</td>
<td>TR/TE/FA=3000/50/90; voxel: 3.75 × 3.75 × 5.5; 25 slices; 120 volumes; 3000</td>
<td></td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>12 Ax GRE Haemoseries</td>
<td>TR/TE₁/TE₂/FA=540/15/67/20; voxel: 0.94 × 0.94 × 4.0; 25 slices; 50</td>
<td></td>
<td></td>
<td>√</td>
</tr>
</tbody>
</table>

FSE=Fast spin-echo; FSPGR=Fast spoiled gradient-echo; EP SE=Echo-planar spin-echo; GRE EPI=Gradient-echo echo-planar; IR=Inversion recovery.

- Image acquisitions being analysed in the project:\*
  - Structural 3D Anatomy - 2 × 124 images / subject / wave (series 5 & 6)
  - Diffusion tensor imaging - 750 images / subject / wave (series 9)
  - Resting state fMRI - 6400 images / subject / wave (series 10)

\*Up until now ...

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An example of multimodal MRI recordings

**DTI – diffusion tensor imaging (Series 9)**
- 5 baseline acquisitions
- 25 diffusion sensitizing directions

**fMRI – resting state (Series 10)**
- 8 ½ min

**fMRI – fingertapping (Series 11)**
- 6 min

**3D MRI – anatomy (Series 5 & 6)**

**Haemoseries (Series 12)**
- TE=15 ms
- TE=67 ms
Voxels and their constituents in brain MRI

Scales:
- Microscopic
- **Mesoscopic** [mm][s]
- Macroscopic

"Given these neuro-statistical data, what are the actual contents of a neuroimaging voxel? An examination of the 300 top-cited cognitive fMRI studies suggests that the commonly used in-plane resolution is 9–16 mm², for slice thicknesses of 5–7 mm. The average voxel size before any pre-processing of the data is thus 55 µl (or 55 mm³). Often the effective size is 2–3 times larger due to the spatial filtering that most investigators apply to improve the functional SNR. Less than 3% of this volume is occupied by vessels and the rest by neural elements.

A typical fMRI voxel of 55 µl in size thus contains 5.5 million neurons, 2.2–5.5 x 10¹⁰ synapses, 22 km of dendrites and 220 km of axons."

N.K. Logothetis, Nature 2008 p.875
Image processing workflows - FreeSurfer

Brain segmentation:

- rawavg.mgz
- aseg.mgz
- aseg.mgz

Brain surface reconstruction and cortical parcellation:

- lh.pial
- FreeSurferColorLUT
- FreeSurfer 5.1 & Freeview
The diffusion tensor:

\[
D = \begin{pmatrix}
D_{xx} & D_{xy} & D_{xz} \\
D_{xy} & D_{yy} & D_{yz} \\
D_{xz} & D_{yz} & D_{zz}
\end{pmatrix}
\]

Principal diffusion directions

\[
\mathbf{e}_1 = (\varepsilon_{1x}, \varepsilon_{1y}, \varepsilon_{1z})
\]

Eigen decomposition:

\[
D \varepsilon_1 = \lambda_1 \varepsilon_1 \\
D \varepsilon_2 = \lambda_2 \varepsilon_2 \\
D \varepsilon_3 = \lambda_3 \varepsilon_3
\]

\[
\lambda_1 \geq \lambda_2 \geq \lambda_3 \geq 0
\]

Fractional anisotropy (“white matter integrity”):

\[
FA = \sqrt{\frac{1}{2} \frac{\sqrt{(\lambda_1 - \lambda_2)^2 + (\lambda_1 - \lambda_3)^2 + (\lambda_2 - \lambda_3)^2}}{\sqrt{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}} \\
0 \leq FA \leq 1
\]

Checking goodness of co-registration between Anatomy and DTI (FA)
Image processing workflows - TrackVis

Whole-brain tractography:

Sagittal view

Coronal view

Tract selection:

Corticospinal tract

Forceps anterior

Left

Right

F_anterior

Superior

Inferior

CST

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Image processing workflows - FCON1000 scripts

Graph analysis of resting state functional connectivity:

(Wave 2 & 3: 80 subjects)

Pairwise MIC similarity between 20 time courses - dual regression metaICA.nii template

MIC = Maximal Information Coefficient (Reshef et al., 2011)

Node degree:

MIC

Mean adjacency matrix

Node #

Comp # i – spatial part

Comp # j – spatial part

Comp # i - temporal part

Comp # j - temporal part
Longitudinal data analysis (LDA) - Linear mixed-effect models

Let $y_{ij}$ denote the response at the $j$th observation of the $i$th subject; $i = 1, \ldots, N$, $j = 1, \ldots, n_i$, and $x_{ij}$ be the corresponding value of the explanatory (covariate) variable $x$, then the standard linear mixed-effects model with random intercept $b_{0i}$ and random slope $b_{1i}$ is:

$$y_{ij} = \beta_0 + \beta_1 x_{ij} + (b_{0i} + b_{1i} x_{ij}) + \epsilon_{ij}$$

- the $\beta_k$s are fixed effect parameters
- the $b_{ki}$s are random effect parameters
- $\epsilon_{ij}$ is the error for observation $j$ in subject $i$, where the errors for subject $i$ are assumed to be multivariate normally distributed
CVLT LongDelay - fit a linear mixed-effect model

Age\textsubscript{ij} as a predictor for \( y_{ij} = \text{LongDelay}_{ij} \) across subjects \( i = 1, \ldots, 106 \) and waves \( j = 1, 2, 3: \quad y_{ij} = \beta_0 + \beta_1 \text{Age}_{ij} + (b_0i + b_1i \text{Age}_{ij}) + \epsilon_{ij} \)
Data organisation (SVN/mySQL - Sebastian Bablock, 2009)
Thanks!

UiB project members

and collaborators:

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