Data Analysis at the Waisman Laboratory: Orientation

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Servers

- Linux servers
  - Dual processor 3 GHz PCs
  - Scientific linux
- Apple
  - Quad-core server running leopard
Disks

• /home: Home directory for users.
  – Old and slow disk drive.
  – Should not be used for image data.
    • Copying large files slows down all computers.
• /apps: Disk where application software is stored.
  – Read-only for users.
• /study: Main data storage disk.
  – 21 TB of disk space.
  – Usually 95-99 % full.
Data Acquisition

- Eprime
- Eye Tracking
- Physiological Data
- Host computer
- Post-processing

/study
Study Outline

1. Design behavioral paradigm.
   - Frame experimental goals in terms of a stimulus-response paradigm.
2. Map behavioral paradigm to MR environment.
   - Optimize statistical power subject to behavioral constraints.
   - Define ancillary goals.
3. Stimulus design.
   - Write Eprime program to generate stimuli.
4. MRI Protocol Design.
   - Coil and pulse sequence selection.
5. Human Studies Approval.
6. Acquire Data.
7. Analyze data.
   1. Preprocess data
   2. Subject-level statistical analysis
Map behavioral paradigm to MR environment

- Determine class of design: block or event-related.
  - Block design repeatedly presents stimuli in blocks of 15-20 seconds followed by blocks of baseline.
  - Event related design present single stimuli followed by a delay of baseline, typically a fixation cross-hair.
- Optimize design with respect to statistical power.
  - Block designs:
    - Equal length blocks, block length less than 20 seconds.
  - Event related designs:
    - Choose optimum timing from among many pseudo-random sequences.
Eprime

- Windows-based program for generating behavioral stimuli.
  - Visual stimuli.
  - Can control other stimuli via digital outputs.
- Triggering Eprime by the scanner.
  - Wait for first RF pulse.
  - Wait for sync pulse at the start of each frame or slice.
- Start scanner from Eprime.
  - Eprime controls the external trigger line to the scanner.
- Program constraints.
  - Must log the start time of the sequence.
Non-MRI Data

- Eye-tracking data.
  - Using Avotec or Magnetic Research systems.
- Physiological data collected on scanner.
  - ECG data acquired with pulse oximeter.
  - Respiratory data acquired from belt.
- Physiological data acquired with Biopac system.
  - EMG.
  - GSR.
  - Adding ECG, respiration, end-tidal CO₂, blood pressure.
Minimal MRI Data Set

- Following images are acquired:
  - $T_1$-weighted structural image(s).
    - Used as an anatomical reference, both within-subject and for normalization to a global template.
  - EPI images.
    - Series of discrete runs.
  - Field-map data.
    - Used to correct EPI images for distortion.
  - DTI data.
    - Used to map white-matter tracts.
  - $T_2$-weighted structural images.
    - Used to improve gray/white segmentation.
Additional MRI Data

• Data are often re-analyzed to test different hypotheses at a later time.

• Additional information can facilitate later analyses.
  – Improved structural images.
    • Additional high-res $T_1$ images.
    • Acquire $T_2$-weighted images for segmentation.
  – Acquire DTI data for structural connectivity.
  – Acquire physiological data.
    • Pulse-oximeter data, respiratory data.
MRI - Image Contrast

• Relies on variations in relaxation rates to create differences in the detected RF.
  – Adjust echo time (TE) for maximum contrast.
• Types of contrast: proton density, $T_1$, $T_2$, and $T_2^*$
  – $T_1$: 1.6/1.2 sec for gray/white matter at 3T
  – $T_2$: 99/60 ms for gray/white matter at 3T
  – $T_2^*$: 40ms, gray matter at 3T
• Choose TE such that the signal difference and absolute signal magnitude are maximized.
T2* and T2 Contrast

MR Signal

T2 Relaxation

90ms for T2 contrast
40ms for T2* contrast
T2-Weighting

- Sequence timing maximizes signal differences between gray and white matter due to $T_2$ relaxation.
- Gray matter is bright.
- White matter is dark.
- At 3T, optimal contrast occurs at approximately $TE=90\text{ms}$.
T1 Contrast

MR Signal

T2 Decay

$S = S_o \cdot (1 - 2 \cdot e^{-T/T1})$

$S = S_o \cdot (1 - 2 \cdot e^{-TE/T1})$

1.1 sec

TI

TE
Inversion Recovery for Extra T1 Contrast

\[ S = S_o \times (1 - 2e^{-t/T1}) \]

\[ S = S_o \times (1 - 2e^{-t/T1'}) \]
T1-Weighting

- Sequence timing maximizes signal differences between gray and white matter due to $T_1$ relaxation.
- Gray matter is dark.
- White matter is bright.
- Can be acquired with a 3D sequence.
- Contrast is a function of TE, TR, inversion time, and flip-angle.
$T_2^*$ Contrast and distortion

- No refocusing pulse.
- Dephasing due to local field variations.
- Susceptibility variations (e.g. in sinuses and ear canals) introduce non-uniformities in the static field along the inferior-superior axis.
- These variations cause variations in signal phase that lead to dephasing across.
- Dephasing causes a spatially varying shift in position in addition to changes in image magnitude.

Gradient Echo Sequence:

<table>
<thead>
<tr>
<th>RF</th>
<th>Readout Gradient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$T$</td>
</tr>
<tr>
<td></td>
<td>TE</td>
</tr>
</tbody>
</table>

$TE = 10\text{ms}$
BOLD Contrast

- **HbO2**: Fraction increases during activation
- **Hbr**: induces local field changes

CBV, FLOW, Field gradients

capillary bed

-2 -1.5 -1 -0.5 0 0.5 1 1.5 2

Percent Change

0 50 100 150 200 250

Time in Seconds

0 10 20 30

Percent Change

0 10 20 30

Time in Seconds
EPI Images

- Sequence Characteristics:
  - GE distortion improves as TE decreases.
  - GE SNR falls as TE decreases. (Fewer lines sampled).
  - SE has better structural fidelity.
Time-Series data - Block Design

- Highest efficiency (statistical power)
- Cannot sort responses.
- Cannot separate signal within a trial.
Time-Series Data: Event-Related Designs

- Widely spaced designs.
  - Less sensitive unless number of stimuli is limited.
- Rapidly presented.
  - “Random” intervals between stimuli.
  - More sensitive, more appropriate behavioral.
  - Timing should be optimized before the experiment.
Model for the Noise

- Stimuli, Baseline
- Neuronal Firing
- Vasculature
- HRF
- BOLD
- Coil-Rcwr
- Bulk, cardiac, respiratory motion, MR instabilities
- Thermal Noise
- Image Data
Motion: Acquisition Slice Order

- Data acquired in axial plane.
- TR/2 time interval between separation of odd and even slices
- ~55% of signal recovered in 1 sec, ~70% in 2 sec, 7% in 135ms
- Adjacent slices in have different steady-state magnetizations.
Motion: Effect of Rotation

- Odd slices
- Even slices

• A two degree rotation alters slice definition and destroys steady-state.
• Steady-state recovered in 5-6 seconds.
Fieldmap Correction
Basis Functions

- The hemodynamic response to a brief stimuli can be modeled by gamma functions, sums of gamma functions, and Gaussian functions.
First-Level Analysis

Let $h(t) = \alpha u(t)$ where $u(t)$ is a model of the hemodynamic response. Then code $u(t)$ into the design matrix and estimate $a$.

\[
\begin{align*}
y_0 &= \alpha h_0 - m + c + \varepsilon_0 \\
y_1 &= \alpha h_1 - \frac{2}{3}m + c + \varepsilon_1 \\
y_2 &= \alpha h_2 - \frac{1}{3}m + c + \varepsilon_2 \\
y_3 &= \alpha h_3 + c + \varepsilon_3 \\
y_4 &= \alpha h_4 + \frac{1}{3}m + c + \varepsilon_4 \\
y_5 &= \alpha h_5 + \frac{2}{3}m + c + \varepsilon_5 \\
y_6 &= \alpha h_6 + m + c + \varepsilon_6
\end{align*}
\]

\[
\begin{bmatrix}
y_0 \\
y_1 \\
y_2 \\
y_3 \\
y_4 \\
y_5 \\
y_6
\end{bmatrix} =
\begin{bmatrix}
0 & -1 & 1 \\
0.2 & -2/3 & 1 \\
1 & -1/3 & 1 \\
1.5 & 0 & 1 \\
1.4 & 1/3 & 1 \\
.5 & 2/3 & 1 \\
.1 & 1 & 1
\end{bmatrix}
\begin{bmatrix}
\alpha \\
m \\
c
\end{bmatrix} +
\begin{bmatrix}
\varepsilon_0 \\
\varepsilon_1 \\
\varepsilon_2 \\
\varepsilon_3 \\
\varepsilon_4 \\
\varepsilon_5 \\
\varepsilon_6
\end{bmatrix}
\]

\[
Y = Ab + \varepsilon
\]
Second Level Analysis

- Regression is mathematically similar to the first-level analysis, but is done across subjects rather than within subjects.
- Incorporates physiological and behavioral data.
  - Reaction time, Tanner score etc.
- Can be a t-test, regression analysis or anova
- Can be done at the voxel-level or regional level.
  - Region level has higher statistical power.
- Classified according to how variance is modeled.
  - Fixed-effect model: Assumes group and subject level variances are equal.
    - No longer used.
  - Random-effects model: Lumps variance into subject level variance.
    - Straightforward t-test, anova, regression analysis.
  - Mixed-effects model: Models both subject and group level variances.
    - FSL, fmristat, SPM, R
Multiple Comparisons

- Voxel level analyses consist of $10^6$ univariate tests.
- Straightforward Bonferroni correction requires $p<5\times10^{-8}$
- Several methods for attaining more reasonable thresholds.
  - Threshold spatial extent as well as probability.
    - Gaussian random field methods.
    - Monte Carlo simulation.
  - False Discovery Rate (FDR)
  - Permutation testing.
Preprocessing

• Uses an automated program, “preprocess”.
• Does the following:
  – Convert to images to neuroimaging formats.
  – Slice time and motion correction (3dvolreg).
  – Fieldmap correction.
• Saves data in a standard directory structure.
Available Packages

• AFNI
  – Great graphical display.
  – Minimal statistical thresholding method.
  – Second level models do not account for first-level variances.

• SPM
  – Excellent interface.
  – Good statistical methods for the most part.
  – Reliance on Bayesian models that are not transparent.
Available Packages

- **fmristat**
  - Excellent statistical techniques.
  - No visualization software.

- **FSL**
  - Good statistical methods
    - Second level analysis accounts for subject-level variance but not in a sophisticated way.
  - Good visualization software but largely dependent on web browsers. (difficult to export results)
  - Supports DTI analysis, independent components analysis.
  - Software can have rough edges.
Resources for Help

• Email list-servers for major packages:
  – AFNI: http://afni.nimh.nih.gov/afni/community
  – FSL: http://www.fmrib.ox.ac.uk/fsl/fsl/support.html
  – SPM: http://www.fil.ion.ucl.ac.uk/spm/support/

• Methods list
  – Email me to join: ollinger@wisc.edu
  – Don’t email me personally, email the list.
  – Most questions are answered by more experienced students and post-docs. Staff members will ensure that all questions are answered.

• Personal contacts: Terry Oakes, John Ollinger, Andy Alexander
  – Please contact us while designing a new study.
    • It is very easy to design a suboptimal or non-analyzable study.