Combining fMRI, ERP and SNP data with ICA: Introduction and examples

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Outline

• Motivation
• Data Description
  • fMRI
  • ERP
  • Genetic
• Features & Joint Estimation
• Joint ICA
  • Example 1: ERP/fMRI
  • Example 2: Multielectrode ERP/fMRI
• Parallel ICA
  • SNP/FMRI
  • SNP/ERP
• Conclusions
Multimodal Data Collection

Brain Function (spatiotemporal, task-related)

Brain Structure (spatial)

Genetic Data (spatial/chromosomal)

Covariates (Age, etc.)

EEG

fMRI

T1/T2

DTI

SNP

Gene Expression

Other*

Task 1-N

Task 1-N
A Role For Data Fusion?:

- EEG
- fMRI

**Comparison:**
- Temporal Resolution: lower for EEG, higher for fMRI
- Spatial Resolution: lower for EEG, higher for fMRI
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- **Joint ICA**
  - Example 1: ERP/fMRI
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- **Parallel ICA**
  - SNP/FMRI
  - SNP/ERP
- **Conclusions**
EEG/ERP
Event-related Potentials (ERPs)
Genetic Variation

ACTTGCATCCG
ACTTGTATCCG
ACTTGCATCCG
ACTTGG--TCCG
ACTTGGCGCGCTCCG
ACTTGGCGC--TCCG
ACTTGGC--TCCG
ACTTTG

Single Nucleotide Polymorphism (SNP)

Insertion/Deletion (Indel)

Short Tandem Repeat (STR)

SUBJECTS

SNP data matrix

SNPS
The Link between brain function and genetic coding
The First Challenge
A conceptual slide to drive home the point…

Gene

mRNA

Protein

Cell

Cell Interaction

Brain Function

Neuroimaging

Behavioral Component

Behavioral Disorder
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Separate vs. Joint Estimation

Linear mixtures with shared mixing parameters

\[ x_{i,v}^{(E)} = \sum_{c=1}^{C} a_{ic} s_{c,v}^{(E)} \quad \text{and} \quad x_{i,v}^{(F)} = \sum_{c=1}^{C} a_{ic} s_{c,v}^{(F)} \]

In a non-joint analysis, we maximize the likelihood functions for each modality separately...

Resulting in two unmixing parameters, that then have to somehow be fused together

In contrast: for a joint analysis we maximize the joint likelihood function, resulting in a single fused unmixing parameter

\[ p(x^{(E)}; w) \quad p(x^{(F)}; w) \quad w = 1 / a \]

\[ w_1^* = \arg \max_{w_1} \log p(x^{(E)}; w_1) \]

\[ w_2^* = \arg \max_{w_2} \log p(x^{(F)}; w_2) \]

\[ w^* = \arg \max_{w} \log p(x^{(E)}, x^{(F)}; w) \]
Feature Data

• **What is a feature?**
  - Lower dimensional data containing information of interest
  - Examples: An image of activation amplitudes, A gray matter segmentation image, fractional anisotropy image

• **Advantages**
  - Less-computationally complex/easier to model
  - Takes advantages of existing analytic approaches
  - Can be used to examine inter-relationships between multiple data types at the subject level
Feature Data

- **What are the features?**
  - Examples: An image of activation amplitudes, a gray matter segmentation image, fractional anisotropy image

- **Advantages**
  - Less-computationally complex/easier to model
  - Takes advantages of existing analytic approaches
  - Examines inter-subject covariation of multiple data types

---

**Modality** | **Core-Feature**
--- | ---
fMRI SB task | Recognition related activity
fMRI AOD task | Target-related activity
sMRI | GM concentration
EEG AOD task | Target-related ERP
  
---

**Modality** | **Raw data size** | **Feature size** | **Compression ratio**
--- | --- | --- | ---
fMRI | 260 MB | 1.3 MB | 1:200
DTI | 200 MB | 10 MB | 1:20
sMRI | 46 MB | 28 MB | 1:1.6
EEG | 25MB | .45MB | 1:56

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<table>
<thead>
<tr>
<th>Feature</th>
<th>Effect Size (d)</th>
</tr>
</thead>
</table>
fMRI | 2.1 (SB Encode) |
sMRI | 0.6 (GM) |
DTI | 0.8 (FA) |
ERP | 2.2 (Target Cz) |
Possible approaches for joint analyses

• Voxel-based
  • Correlation [Worsely 1998]
  • *Straightforward, but difficult to visualize*

• Region-based
  • Interregional correlation [Horwitz, et al, 1984]
  • Structural equation modeling [McIntosh and Gonzalez-Lima 1994; Friston et al., 2003, McIntosh & Gonzalez-Lima, 1991, Buchel & Friston, 1997]
  • Multiple regression and extensions [e.g., Kalman filters, Buchel & Friston, 1998]
  • *Useful for model testing, does not take into account all brain regions*

• Transformation-based
  • *A natural set of tools for this problem include those that transform data matrices into a smaller set of modes or components*
  • Singular value decomposition [Friston et al., 1993; Friston et al., 1996]
  • Partial Least Squares [McIntosh, Bookstein, et al, 1996]
  • Canonical Variates Analysis [Strother et al, 1995]
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\[
\begin{bmatrix}
  x_{\text{mod } 1} \\
  x_{\text{mod } 2}
\end{bmatrix}
= \mathbf{A} \times 
\begin{bmatrix}
  s_{\text{mod } 1} \\
  s_{\text{mod } 2}
\end{bmatrix}
\]
Blind Source Separation (ICA)

ICA finds directions which maximize independence (using higher order statistics)
Stationarity

Consistency of Stationary ICA

Correlation

fMRI  ERP  SNP  Behavioral

Healthy  Patient

Infomax ICA vs TFBSS

Correlation

fMRI Component  fMRI Mixing Matrix  ERP Component  ERP Mixing Matrix

Comp1  Comp2  Comp3  Comp4
a  
**Joint ICA**  
*Shared Feature Profile*

- **Coupled feature matrix**  
  - Participant  
  - Voxel/time courses  
  - Feature 1  
  - Feature 2  
- **Source matrix**  
  - Map 1  
  - Map 2  
  - Weights  

b  
**Parallel ICA**  
*Distinct but linked Feature Profile*

**Data1 Initialization**  
\( (\lambda_1, \lambda_{c1}) \)

- Update \( W_1 \) based on \( H_1 \)
- Stop ?
- Y  
- N  
- Update \( W_1 \) based on Correlation

**Data2 Initialization**  
\( (\lambda_2, \lambda_{c2}) \)

- Update \( W_2 \) based on \( H_2 \)
- Stop ?
- Y  
- N  
- Update \( W_2 \) based on Correlation

**Select the related components**
Joint ICA

\[
\begin{bmatrix}
X_{\text{mod 1}} \\
X_{\text{mod 2}}
\end{bmatrix}
= \mathbf{A} \times \begin{bmatrix}
S_{\text{mod 1}} \\
S_{\text{mod 2}}
\end{bmatrix}
\]

Generative Model:
\[
\begin{bmatrix}
x_i^F \\
x_i^E
\end{bmatrix} = \mathbf{A} \begin{bmatrix}
S_c^F \\
S_c^E
\end{bmatrix}
\]

Update Equation:
\[
\Delta \mathbf{W} = \eta \left\{ \mathbf{I} - 2y^F \left( \mathbf{u}^F \right)^T - 2y^E \left( \mathbf{u}^E \right)^T \right\} \mathbf{W}
\]


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Peak of “Target”-locked fMRI signal

Position Cz of “Target”-locked EEG signal

Subject 1
Subject 2
Subject N

jICA

Noise Removal

Visualization

Preprocess

FMRI

Feature Extraction

EEG

Feature Extraction

Normalize

Normalize
Joint ERP/fMRI Components

ERP (temporal) Components: \( T = [t_1 \ldots t_N] \)

FMRI (spatial) Components: \( S = [s_1 \ldots s_N] \)

FMRI Image Snapshot: \( M_F (t) = |T| \times S^T (t) \)

ERP Snapshots

ERP (temporal) Components: \( \mathbf{T} = [t_1, \ldots, t_N] \)

FMRI (spatial) Components: \( \mathbf{S} = [s_1, \ldots, s_N] \)

ERP Timecourse Snapshot: \( \mathbf{M}_E (\nu) = \mathbf{T} \times |\mathbf{S}|^T (\nu) \)

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fMRI/SNP connection

• fMRI component: *specific brain regions with common independent brain functionality.*

• SNP component: *a linearly weighted group of SNPs functioning together.*

• Relationship assumption
  
  If an association of SNPs partially define a certain brain function in specific brain regions, Then, the linked fMRI and SNP components should share a similar pattern of existence across subjects.
Parallel ICA structure

Data1: (fMRI)  
Data2: (SNP)

\[ \text{MAX : } \{H(Y_1) + H(Y_2)\}, \text{ Infomax} \]

Subject to: \( \text{arg max } g\{W_1, W_2 \mid s_1, s_2\} \),

\[ g(\cdot) = \text{Correlation}(A_1, A_2)^2 = \frac{\text{Cov}(a_{i1}, a_{j2})^2}{\text{Var}(a_{i1}) \times \text{Var}(a_{j2})} \]
Dynamic parallel ICA optimization

- Dynamically constrained components:
  \[ X_1 \rightarrow \hat{S}_1 \quad X_2 \rightarrow \hat{S}_2 \]

- Adaptive constraint strength:
  - Effects on Entropy \( H(.) \)
Simulation data

- DATA1
- A1

<table>
<thead>
<tr>
<th>Data1</th>
<th>Data2</th>
<th>Parallel ICA connection</th>
<th>Regular ICA connection</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>4</td>
<td>0.4149</td>
<td>0.4148</td>
</tr>
<tr>
<td>8</td>
<td>8</td>
<td>0.8275</td>
<td>0.6635</td>
</tr>
<tr>
<td>16</td>
<td>8</td>
<td>0.8240</td>
<td>0.6639</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>0.1739</td>
<td>0.1738</td>
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<tr>
<td>8</td>
<td>8</td>
<td>0.8492</td>
<td>0.6636</td>
</tr>
<tr>
<td>16</td>
<td></td>
<td>0.8953</td>
<td>0.6636</td>
</tr>
</tbody>
</table>

True component: 8/8; True correlation: 0.8

<table>
<thead>
<tr>
<th>True Correlation</th>
<th>Parallel ICA correlation</th>
<th>Regular ICA correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.00</td>
<td>0.9278</td>
<td>0.8606</td>
</tr>
<tr>
<td>0.80</td>
<td>0.7911</td>
<td>0.7348</td>
</tr>
<tr>
<td>0.60</td>
<td>0.5850</td>
<td>0.5205</td>
</tr>
<tr>
<td>0.45</td>
<td>0.4603</td>
<td>0.4138</td>
</tr>
</tbody>
</table>
Parallel ICA

1. independent components/factors of each modality
2. Inter-relationship between modalities

The algorithm is based on classic ICA, aiming to extract independent sources and enhance the connections between modalities.
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Example 1: SNP/fMRI Fusion

Data Description: 20 Sz & 43 Healthy controls (Caucasian)
  fMRI: one image per subject (Target activation in Auditory Oddball task
  SNP: one array per subject (384 SNP genotypes - > 367 SNPs)

Control vs Patient
p<0.001

<table>
<thead>
<tr>
<th>SNP</th>
<th>Z score</th>
<th>Gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rs1466163</td>
<td>-4.08</td>
<td>AADC: aromatic L-amino acid decarboxylase</td>
</tr>
<tr>
<td>Rs2429511</td>
<td>3.97</td>
<td>ADRA2A: alpha-2A adrenergic receptor gene</td>
</tr>
<tr>
<td>Rs3087454</td>
<td>-3.09</td>
<td>CHRNA7: alpha 7 nicotinic cholinergic receptor</td>
</tr>
<tr>
<td>Rs821616</td>
<td>2.96</td>
<td>DISC1: disrupted in schizophrenia 1</td>
</tr>
<tr>
<td>Rs885834</td>
<td>-2.78</td>
<td>CHAT: choline acetyltransferase</td>
</tr>
<tr>
<td>Rs1355920</td>
<td>-2.77</td>
<td>CHRNA7: cholinergic receptor, nicotinic, alpha 7</td>
</tr>
<tr>
<td>R4765623</td>
<td>2.73</td>
<td>SCARB1: scavenger receptor class B, member 1</td>
</tr>
<tr>
<td>Rs4784642</td>
<td>-2.71</td>
<td>GNAO1: guanine nucleotide binding protein (G protein),</td>
</tr>
<tr>
<td></td>
<td></td>
<td>alpha activating activity polypeptide O</td>
</tr>
<tr>
<td>Rs2071521</td>
<td>2.58</td>
<td>APOC3: apolipoprotein C-III</td>
</tr>
<tr>
<td>Rs7520974</td>
<td>2.55</td>
<td>CHRM3: muscarinic-3 cholinergic receptor</td>
</tr>
</tbody>
</table>

Subject loading associated with linked SNP and fMRI components
Sample size vs Number of SNPs

Data collected at UCI
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Example 2: Genetics and P3 ERP generation

- Subjects: 41 healthy subjects (24 female, 17 male)
- EEG collected during AOD task, target/novel ERPs extracted
- Blood sample collected, genotyped 384 SNPs from 222 genes 6 physiological systems.
Fusion ICA Toolbox (FIT)

Fusion ICA Toolbox (FIT)
FITv2.0a

Methods:

Parallel ICA
Joint ICA

About Help Exit

Group Average Histograms

ERP AOD Activity
fMRI AOD Activity

Control
Patient

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