Outline of Talk

- Approaches
  - Seeds vs Components
  - Intro to ICA
  - Group ICA vs single subject
- Processing issues
  - Impact of (micro) motion
  - Autocorrelation
  - Band-pass filtering
- Other issues
  - Task vs Rest
  - Overlap of networks
- Applications
  - Diagnostic
  - Prediction
  - Dynamic connectivity
- Summary


Seeds vs Components

- Seed approaches
  - Require one or more seed regions
  - Involved univariate cross-correlation
  - Require filtering
  - Require some measure of removal of physiologic noise (covary w/ physiologic noise or white/csf regions)
  - Full correlation vs partial correlation is an important decision
- Independent component analysis (ICA)
  - Fully data-driven (no seed region, though priors are possible)
  - Assumes linear covariation within components
  - Assumes linear mixing among components
  - Maximizes spatial independence
  - All components have values at all voxels (enabling spatial filtering of artifacts and overlapping components)


ICA vs PCA

Uncorrelated: $E[y_1 y_2] = E[y_1]E[y_2]$

Independent: $p(y_1, y_2) = p(y_1)p(y_2)$

$\Rightarrow E[h(y_1)h(y_2)] = E[h(y_1)]E[h(y_2)]$

PCA finds directions of maximal variance (using second order statistics)

ICA finds directions which maximize independence (using higher order statistics)
We can evaluate the component timecourses

\[ y(j) = \hat{\beta}_0 + \sum_{i} \hat{\beta}_i x_i(j) + e(j) \]

1. Model (1 or more Regressors)
2. Data
3. Fitting the Model to the Data at each voxel

ICA Halloween (Un)Mixer!

\[ X = A \times S \]

Consistency of ICA Algorithms

Group ICA

Assessing Task Modulation of Components

- We can evaluate the component timecourses within a standard GLM approach.
For each subject, each selected component can be included or not, be translated and rotated in space, and the spatial spread of the component can be increased or decreased. Each SM is normalized to have a peak-to-peak amplitude range of one.

- Roughly 30 SMs can be selected through the graphical user interface by clicking on components, or by component number in the batch script.

For each subject, each selected component can be included or not, be translated and rotated in space, and the spatial spread of the component can be increased or decreased. Each SM is normalized to have a peak-to-peak amplitude range of one.


http://mialab.mrn.org/software/simtb


http://coins.mrn.org

Multivariate Testing Framework

univariate models
(1) $H_0: \beta_1 = 0$
(2) $H_0: \beta_i = 0$

Is voxel $i$ affected by age?

multivariate models
$H_0: \beta_1 = \beta_2 = \ldots = \beta_v = 0$

Are any of these voxels affected by age?

Is voxel $i$ affected by age?

Rapid Imaging (multiband EPI)

TR=275ms, 39 subjects

Seed vs Components
- Once fixed they are very similar
  - “Seed-based FC measures are shown to be the sum of independent component analysis-derived within-network connectivities and between-network connectivities” Joel SE, Collin BS, van Zijl PC, Pekar JJ. On the relationship between seed-based and ICA-based measures of functional connectivity. Mag Reson Med. 2011 Sep;66(3):644-57
  - ICA/seed hybrid (use ICA to derive seed regions or maps)
  - Spatially constrained approach

On ICA Model Order: Reconstruction of low model order from high model order

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**Impact of motion on FNC**

We selected 3 sets of subjects (total N = 219):
- **Non-Movers (NM):** Subject group who had very small framewise micromovements (FD) at r < 0.2
- **Continuous Movers (CM):** Subject group who had continuous framewise micromovements of 2 mm or higher (more micromovements) (NM = 76)
- **Small Movers (SM):** Subject group who had reasonable framewise micromovements but with occasional very high movements of FD at r > 0.2 (NM = 68)

**High-Frequency: Baby vs Bathwater?**

<table>
<thead>
<tr>
<th>Description</th>
<th>Corr</th>
<th>FD_rms Mean</th>
<th>FD_rms Med</th>
<th>Micromovements</th>
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<tbody>
<tr>
<td>No motion</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Continuous</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Jerky</td>
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**Autocorrelation**

Uncorrected vs Corrected

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  - Small vs Compromised
  - Into to ICA
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**Task vs Rest**

Result 1: AOD and rest data produced highly similar networks

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<td>AOD</td>
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<tr>
<td>REST</td>
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Result 2: Though similar TCNs were identified for AOD and rest, spatial and temporal task modulation was induced

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Effect of Task on Intrinsic Networks in SZ vs HC

Controls show significantly higher connectivity than patients at all tasks. Patients show significantly higher connectivity than controls at all tasks. Patients show significantly higher connectivity than controls in the resting state and controls show significantly higher connectivity than patients at other tasks. Controls show significantly higher connectivity than patients in the resting state and patients show significantly higher connectivity than controls at other tasks. Controls show significantly higher connectivity than patients in the resting state and neither patients nor controls show significantly higher connectivity at other tasks. Patients show significantly higher connectivity than controls in the resting state and neither patients nor controls show significantly higher connectivity at other tasks.

Stable Across Tasks
Variable Across Tasks

Overlap of Networks

Task-positive
Task-negative

Concurrent EEG/fMRI: eyes open vs eyes closed

These results suggest that changes in neuronal synchronization as indicated by power fluctuations in high-frequency (>1Hz) EEG rhythms such as posterior alpha are partly mediated by widespread changes in inter-regional low-frequency (<.1Hz) functional activities detected in fMRI. They also indicate that generation of local hemodynamic responses is highly sensitive to global state changes that do not involve changes of mental effort or awareness.


fBIRN SIRP Task

Methods
• Subjects & Task:
  • 28 subjects (14 HC/14 SZ) across two sites
  • Three runs of SIRP task preprocessed with SPM2
• ICA Analysis
  • All data entered into group ICA analysis in GIFT
  • ICA time course and image reconstructed for each subject, session, and component
  • Images: sessions averaged together creating single image for each subject and component
  • Time courses: SPM SIRP model regressed against ICA time course
• Statistical Analysis:
  • Images: all subjects entered into voxelwise 1-sample t-test in SPM2 and thresholded at t=4.5
  • Time courses: Goodness of fit to SPM SIRP model computed, beta weights for load 1, 3, 5 entered into Group x Load ANOVA

fBIRN Phase II Data: www.nbirn.net; NCRR (NIH), 5 MOI RR 000827 (2002-2006) and 1 U24 RR0219921 (2006 onwards)

Component 1: Bilateral Frontal/Parietal

Component 2: Right Frontal, Left Parietal, Post. Cing.
Component 3: Temporal Lobe

Relationship to Disease (N=1140)

Healthy (N=590)
Substance Use (N=469)
Schizo/BP (N=81)

Between network example: precuneus-cerebellar connectivity

Within network example: anterior DMN

Robustness of ‘modes’

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3-way Classification of Schizophrenia, Bipolar, Control

1) Remove subjects from each group

2) Identify regions which maximally separate remainder

3: Develop simple classifier based upon 'distance' between each group:

4) Classify 'left out' participants


1) Remove subjects from each group

2) Identify regions which maximally separate remainder

3: Develop simple classifier based upon 'distance' between each group:

4) Classify 'left out' participants


Diagnostic Classification: FNC

How informative is 5 minutes of resting-state fMRI data?

Separate ICAs performed on training/testing sets, 9 RSNs selected

Features are the temporal correlations between components

Mohammad R. Arbabshirani and Vince D. Calhoun, In submission

Simulated Driving Paradigm

Baseline Simulated Driving Results

Higher Order Visual/Motor: Increases during driving; less during watching.

Low Order Visual: Increases during driving; less during watching.

Motor control: Increases only during driving.

Vigilance: Decreases only during driving; amount proportional to speed.

Error Monitoring & Inhibition: Decreases only during driving; rate proportional to speed.

Visual Monitoring: Increases during epoch transitions.

Mohammad R. Arbabshirani and Vince D. Calhoun, In submission

Previous Work


"Our results suggest that simulated driving engages mainly areas concerned with perceptual-motor integration and does not engage areas associated with higher cognitive functions."

"Our study suggests that the main ideas of cognitive psychology used in the design of cars, in the planning of respective behavioral experiments on driving, as well as in traffic-related political decisions making (i.e., laws on what drivers are supposed to do and not to do during driving) may be inadequate, as it suggests a general limited capacity model of the psyche of the driver which is not supported by our results. If differing doctrines, rather than activate a number of brain regions the quests for the adequate design of the man-machine interface as well as for what the driver should and should not do during driving is still widely open."

Mohammad R. Arbabshirani and Vince D. Calhoun, In submission
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Dynamic FNC

Some FC states show excellent segregation with regard to EO/EC condition.

Most states also show temporal trends, highly consistent with those seen in our previous study.

Perhaps the most notable feature of States 5 and 6, which increase in frequency over time and are much more likely to appear in EC, is the lack of antagonism between the DMN and sensorimotor and/or cognitive control networks.

Mialab Software

- [http://mialab.mrn.org/software](http://mialab.mrn.org/software)
- freeware, written in MATLAB
- **Group ICA of fMRI Toolbox (GIFT)**
  - Single subject/Group ICA
  - MANCOVA testing framework
  - Source-Based Morphometry
  - Model order estimation
  - ICASSO (clustering/stability)
- **Fusion ICA Toolbox (FIT)**
  - Parallel ICA, jICA
  - mICA+jICA & much more!
- **Simulation Toolbox (SimTB)**
  - Flexible generation of fMRI-like data

Structure/Function

- Mapping the Structural Core of Human Cerebral Cortex. Hagman, et al. 2008
  PLOS Biology

  *Structural Core: (For both hemispheres)*
  - Posterior cingulate cortex, precuneus, cuneus, paracentral lobule, isthmus of the cingulate, banks of the superior temporal sulcus, & inferior/superior parietal cortex
Structural (sMRI) components (red) and corresponding rs-fMRI components (blue).

Group ICA of DTI identifies separate microstructures of corpus callosum.

Patient/Control Differences

- Decreased connectivity
- Increased connectivity

Graph Theory

- Correlation Matrix
- Adjacency Matrix

Patient/Control Differences

- P < 0.05 FDR corrected
- Age effect removal
- Cluster size > 5 voxels

Qingbao’s stuff???

FNC variability

- A "zone of instability" (ZOI) is apparent between dorsal attention areas, parietal default mode regions, and superior parietal cortex.
Markov modeling

Independence appears to be a useful way to identify states

Functional connectivity: the first study

seed-based correlation maps

Overview

Motivation
Simulations
Studying with large N healthy dataset
Converging evidence with concurrent EEG/fMRI
Application to Schizophrenia
Ongoing work
Conclusions

A couple definitions

Connectome
Scale (Macro/Meso/Micro)
Function vs Structure

Network
Context determines the meaning and interpretation of the word "network" in brain imaging analysis.
GLM and seed-based method define a network as a subset of voxels whose timeseries are significantly correlated with a reference signal.
Using graph theory, a network may be defined as a connectivity matrix between nodes, which represent voxels, areas, or components.
ICA provide a description of the relationships among all voxels.
FNC is a network of networks (e.g. graph theory or correlations among network timecourses)
Each author should explicitly state the interpretation implicit in the method.


