Practical Issues for Multimodal Neuroimaging
WhynHow 5/5/11

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Multimodal Imaging: Why and How

- Why do it?
- How to design the study
- How to approach data analysis
- Why don’t the datasets match up??
Why do it?
Why do it?

• Combine the strengths of each technique to attack a problem
  • E.g. the holy grail: space+time
fMRI

- Measure differences in BOLD associated with different stimulus or task evoked processes
- Slow, non-temporally specific
- Fairly spatially accurate
**EEG**

- Measure differences in voltage measured at scalp, probably arising from summed post-synaptic potentials
- Temporally precise
- Spatially imprecise
- Cheap, so very well-established literature

*Matti Hamalainen*
MEG

• Measure differences in magnetic field in sensors surrounding head, probably arising from post-synaptic potentials
• Temporally precise
• Some reliable spatial estimates possible

Marinkovic et al.
Why do it?

• Combine the strengths of each technique to attack a problem
  – the holy grail: space+time

**fMRI**
- Precise in space, not time

**MEG**
- Precise in time
- Some spatial information
  - 230-250 ms
  - 300-340 ms

**EEG**
- Precise in time, not space
Why do it?

• Converging evidence
  – E.g. compare spatial estimates from two techniques
Why do it?

• Get a better understanding of the properties of different recording techniques

fMRI

• Precise in space, not time

MEG

• Precise in time
• Some spatial information

230-250 ms

300-340 ms

EEG

• Precise in time, not space
How to design the study
Design

- Separate recording sessions with different subjects
Design

• Separate recording sessions with same subjects

Session 1

fMRI

Session 2

MEG
Design

• Simultaneous recording

EEG

MEG
Design

• Mixed separate and simultaneous
Design

• In deciding which to pursue, must consider
  – Facilities available
  – **Goal** of multimodal component
  – Analysis resources available
  – Constraints of your paradigm
  – Constraints of your subject population
  – How much effort you want to devote to the project!
Design: General

• Stimulus presentation must be reasonably well-matched across techniques
  – Block designs

Doug Greve
Design: General

- Stimulus presentation must be reasonably well-matched across techniques
  - Block designs
    - Could work for EEG/MEG if you are looking at steady-state responses, i.e. whether power in a certain frequency band is different for A blocks and B blocks
    - Won’t work if you are looking at stimulus evoked responses in EEG/MEG
Design: General

• Stimulus presentation must be reasonably well-matched across techniques
  – Event-related designs: EEG/MEG

Luck 2005
Design: General

• Stimulus presentation must be reasonably well-matched across techniques
  – Event-related designs: fMRI

Doug Greve
Design: General

• Stimulus presentation must be reasonably well-matched across techniques
  – Special requirements for stimuli in event-related fMRI
    • To get the most robust estimates, need to optimize order of stimulus presentation such that sequence is not completely random (e.g. ‘optseq’ software)
    • Need to add ‘null’ periods of fixation for fMRI deconvolution
Design: General

• Stimulus presentation must be reasonably well-matched across techniques
  – Special requirements for event-related stimuli in MEG/EEG
    • Regular rest intervals for people to blink
    • May need a larger number of trials to estimate source solutions
Design: General

• Stimulus presentation must be reasonably well-matched across techniques
  – Matching visual angle, resolution, and other low-level properties across very different projection setups
  – And so on...
Design

• Run two separate experiments yourself
• Do a post-hoc comparison of previous results
Between-Subjects Design

• Need to have enough subjects for it to be reasonable to generalize to (sub)population
  – For MEG, EEG, and fMRI, personal rule of thumb is about 16 good subjects drawn from approximately same age-range and educational level
  – Should be recruited in the same way
Design

- Separate recording sessions with same subject

Session 1

MRI

Session 2

MEG
Within Subjects

• Effects of repeating paradigm
  – Practice effects on task performance
  – Memory effects (for higher-level cognitive paradigms)
  – Psychological effects (arousal, fear, attention)

• Effects of repeating stimuli
  – If you repeat, memory effects
  – If you don’t repeat, not exactly same experience
  – If not repeating, need twice as many!
Within Subjects

• Counterbalancing, counterbalancing...
  – Order of measures (fMRI-MEG, MEG-fMRI) most important
  – Order of stimuli lists (if different)
  – List x measure interaction?
  – Can be difficult because of limited sample size

• Controlling delay between Session 1 and Session 2?
  – Can be difficult because of logistics!
Within Subjects

• Participants
  – Double the possible exclusion factors
    • E.g. metal fillings for MEG, vertigo/claustrophobia/body size for fMRI
  – Participant scheduling
    • ‘Need someone who can make it to our lab’s Thursday 2-4 MRI slot and our Monday 10-1 MEG slot’
  – Participant drop-out
    • Spend 1k on the fMRI and they don’t return for MEG!
  – Uneven data quality
    • Subject keeps still in the MRI but moves a lot in MEG
Within Subjects

• Participants
  – Inevitably, you will end up with participants that have one good dataset but not the other, so try to design experiment in such a way that data from each technique by itself is still valuable
Design

- Simultaneous recording

EEG  MEG
Simultaneous Recording

• Recording is more difficult and more prone to error
  – More steps to remember, more pieces of equipment, more chances something will go wrong on a given day
    • Extreme organization is absolutely necessary!
  – Participants may become more anxious or bored during a long setup
Simultaneous Recording

- One measure may cause artifact in the other
  - E.g. simultaneous fMRI-EEG
- Or pain
  - E.g. electrodes pressing into the back of subject’s head
How to approach the analysis
Summary

• In deciding which design to pursue, must consider
  – Facilities available
  – **Goal** of multimodal component
  – Analysis resources available
  – Constraints of your paradigm
  – Constraints of your subject population
  – How much effort you want to devote to the project!
Analysis

• Now you have two (or more) datasets: how do you integrate them?
  – Often uncharted territory!
  – Could just try to do an automatic combination in some fancy software package
    • E.g. Combine MEG+EEG data to do source localization and use fMRI as a constraint in MNE package
  – However, this kind of sight-unseen analysis is risky and unlikely to work
    • Think about matching your datasets before you integrate them
Cond B – Cond A

<table>
<thead>
<tr>
<th>fMRI</th>
<th>MEG/EEG</th>
</tr>
</thead>
<tbody>
<tr>
<td>154 Ventrolateral prefrontal cortex</td>
<td>200-220 ms centroparietal</td>
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## Cond B – Cond A

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<tbody>
<tr>
<td>154  L Ventrolateral prefrontal cortex</td>
<td>200-220 ms centroparietal negativity</td>
</tr>
<tr>
<td>103  Anterior cingulate</td>
<td>340-500 ms frontal positivity</td>
</tr>
<tr>
<td>91   R supramarginal gyrus</td>
<td>??</td>
</tr>
<tr>
<td>24   L cerebellum</td>
<td></td>
</tr>
</tbody>
</table>

*Note: The entry for the R supramarginal gyrus in EEG has been crossed out.*
Analysis

• Matching up datasets
  – Event-related analyses in EEG/MEG usually interpreted in windows of 10-300 ms duration
  – fMRI: one picture summing all effects in >2 s window
Analysis

• Matching up datasets
  – Start with prior knowledge

Lau et al 2008
Analysis

• Matching up datasets
  – Covariation across multiple manipulations

• Long prime-target asynchronies
  • Reduced N400 amplitude in ERP
  • Reduced BOLD in IFG and MTG

• Short prime-target asynchronies
  • Reduced N400 amplitude in ERP
  • Reduced BOLD in MTG only
Analysis

• Matching up datasets: within-subjects designs
  – Can take advantage of within-subjects nature of the design with individual subject analyses, e.g.
    • Lateralization index in each measure
    • Location of activity in the individual relative to the group average, in each measure
    • Correlations in effect size in each measure across individuals
Analysis

• Matching up datasets: within-subjects designs
  – If you can figure out a reliable means of matching up the two datasets, you can now use one measure to aid in source localization for the other measure on an individual basis (i.e., fMRI as a constraint on MEG/EEG source localization)
Analysis

• Matching up datasets: simultaneous recording
  – Can take advantage of the fact that you have simultaneous data from individual trials—but how?
Analysis

• Matching up datasets: simultaneous recording
  – Correlation analyses over individual trials
    • Note that many software programs may not be specialized to access individual trial information
    • Also have to decide what correlations to look for, and what will count as a meaningful correlation
Summary

- Plan analysis ahead!
A few references to get started...

- Sharon et al. (2007) *Neuroimage* – fMRI + MEG/EEG within subjects
- Ahveninen et al. (2006) *PNAS* – fMRI + MEG within subjects
- Vartiainen et al. (2011) *J. Neurosci* – fMRI + MEG/EEG within subjects
- Kveraga et al. (2011) *PNAS* – fMRI + MEG in frequency domain, partly within subjects
- Ahveninen et al. (2011) *PNAS* – fMRI + MEG/EEG
Why might measures differ?
Accounting for Differences

• Different spatial sensitivity profiles
  – MEG not very sensitive to deep sources, best for sulci
  – EEG may suffer from increased source cancellation
  – fMRI areas of significant artifact such as anterior medial temporal cortex
Accounting for Differences

• Different temporal sensitivity profiles
  – fMRI sums across time, so better at picking up small effects with a long duration, or effects with less precise onsets relative to stimulus presentation
  – Event-related MEG/EEG in the time domain does not sum across time, so good at picking up short-lasting effects with a precise onset relative to stimulus presentation
  – Frequency analysis of MEG/EEG across larger time windows may be closer to fMRI in temporal sensitivity
Accounting for Differences

• Matching up datasets
  – Different levels of background variability
    • E.g., in sentence comprehension in fMRI, pulling out brain area involved in fixing violations versus area involved in lexical access
Example

The boy was flying a kite

‘Fixing-Violations’ Brain Area

The boy was flying a kite pickle

EEG/MEG
Example

The boy was flying a kite glider.

Lexical Access Brain Area

EEG/MEG

The boy was flying a kite glider.
A few ‘mismatch’ references

• Vartiainen et al., 2011, *J. Neurosci.*
• Yigal Agam (submitted)
• Brem et al., 2009, *Hum. Brain Mapp.*
Multimodal Neuroimaging is difficult...

• Don’t need to be an expert in each modality
  – But good to have an expert *consultant* for each
• Do need a lot of foresight, organization, and planning
  – Not a ‘tack-on’
• Few cookie-cutter analysis routines available, so analysis needs to be planned ahead
...but rewarding!

- Can have great payoffs in better understanding both system of interest and the measures themselves