Practical Intensity-Based Meta-Analysis

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OHBM Neuroimaging Meta-Analysis Educational course
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Coordinate- or Image-Based?

Experiment → Acquisition → Raw data → Analysis → Results → Publication → Paper
Coordinate- or Image-Based?

Coordinate-based meta-analysis
Coordinate- or Image-Based?

Coordinate-based meta-analysis

Image-based meta-analysis
Image-based meta-analysis how to?
Image-based meta-analysis

Subject 1

Pre-processed data → Model fitting and estimation → Contrast and std. err. maps → Inference → Detections (subject-level)
Image-based meta-analysis

```
Subject 1
Pre-processed data → Model fitting and estimation → Contrast and std. err. maps → Inference → Detections (subject-level)

Subject n
Pre-processed data → Model fitting and estimation → Contrast and std. err. maps → Inference → Detections (subject-level)
```
Image-based meta-analysis

Subject 1

Pre-processed data → Model fitting and estimation → Contrast and std. err. maps

Subject n

Pre-processed data → Model fitting and estimation → Contrast and std. err. maps

Model fitting and estimation → Inference → Detections (study-level)
Inference

Detections (study-level)

Image-based meta-analysis

Subject 1

Pre-processed data

Model fitting and estimation

Contrast and std. err. maps

Model fitting and estimation

Contrast and std. err. maps

Inference

Detections (study-level)

Subject n ...

Pre-processed data

Model fitting and estimation

Contrast and std. err. maps

Model fitting and estimation

Contrast and std. err. maps

Inference

Detections (study-level)

Subject 1

Pre-processed data

Model fitting and estimation

Contrast and std. err. maps

Model fitting and estimation

Contrast and std. err. maps

Inference

Detections (study-level)

Subject n ...

Pre-processed data

Model fitting and estimation

Contrast and std. err. maps

Model fitting and estimation

Contrast and std. err. maps

Inference

Detections (study-level)
Image-based meta-analysis

- Subject 1
  - Pre-processed data
  - Model fitting and estimation
  - Contrast and std. err. maps

- Subject n
  - Pre-processed data
  - Model fitting and estimation
  - Contrast and std. err. maps

- Model fitting and estimation
  - Contrast and std. err. maps

Inference
  - Detections (meta-analysis)
Image-based meta-analysis
Image-based meta-analysis

• Gold standard:
  
  **Third-level Mixed-Effects GLM**

• Requirements
  – study-level **Contrast estimates** and **Standard error maps**.
  – Same **units**
Units of contrast estimates

Pre-processed data → Model fitting and estimation → Contrast and std. err. maps
Units of contrast estimates

- Pre-processed data
- Data scaling
- Scaled pre-processed data
- Model parameter estimation
- Parameter estimates
- Contrast estimation
- Contrast and std. err. maps
Units of contrast estimates

\[
\text{scaled}_\text{data} = \frac{\text{data} \times \text{target}}{\text{est}_\text{mean}}
\]

Units depend on **mean estimation** and **scaling target**.
Units of contrast estimates

$Y = \beta + \epsilon$

Units depend on **scaling** of explanatory variables
Units of contrast estimates

- Contrast Estimation
  - Linear combination of parameter estimates
  - Final statistics invariant to scale
    - e.g. \([1 1 1 1]\) gives same T’s & P’s as \([\frac{1}{4} \frac{1}{4} \frac{1}{4} \frac{1}{4}]\)

Units depend on contrast vector
- Rule for contrasts to preserve units
  - Positive elements sum to 1
  - Negative elements sum to -1
Image-based Meta-analysis

• Gold standard: Third-level Mixed-Effects GLM

• But…
  – Units will depend on:
    • The scaling of the data (subject-level)
    • The scaling of the predictor(s) (subject- and study-level)
    • The scaling of the contrast (subject- and study-level).
  – Contrast estimates and standard error maps are rarely shared…
Which images for IBMA?

### SPM
- **Contrast & std. err. maps**
  - con_0001.nii
  - [SPM.mat]

### FSL
- **Contrast map**
  - con_0001.nii
  - cope1.nii
  - varcope1.nii (squared)

### AFNI
- **Statistic map E.g. Z-map**
  - spmT_0001.nii
  - tstat1.nii.gz
  - zstat1.nii.gz

- **Contrast map**
  - con_0001.nii
  - cope1.nii

- **3dMEMA_result+tlrc.BRIK[[0]]**
  - [from contrast & stat maps]

- **3dMEMA_result+tlrc.BRIK[[1]]**
Image-based meta-analyses based on Z

- **Fisher's**
  \[ -2 \sum_{k} \log P_k \sim \chi^2_{2k} \]
  - Sum of \(-\log P\)-values (from T/Z’s converted to P’s)

- **Stouffer’s**
  \[ \sqrt{K} \times \frac{1}{K} \sum_{k} Z_k \sim \mathcal{N}(0, 1) \]
  - Average Z, rescaled to N(0,1)

- **“Stouffer's Random Effects (RFX)”**
  \[ \sqrt{K} \times \frac{1}{K} \sum_{k} Z_k \sim \mathcal{N}(0, \sigma^2_{RFX}) \]
  - Submit Z’s to one-sample t-test

(Slide adapted from Thomas Nichols, OHBM 2015)
Image-based meta-analyses based on $Z + N$  

- Weighted Stouffer’s  
  \[ \sum_k w_k Z_k \sim \mathcal{N}(0, 1), \quad w_k \propto \sqrt{N_k} \]
  - $Z$’s from bigger studies get bigger weight

(Slide adapted from Thomas Nichols, OHBM 2015)
Image-based meta-analyses based on Con’s

• Random Effects (RFX) GLM

$$\frac{1}{K} \sum_{k} c_\beta_k \sim \mathcal{N}(0, \sigma_{RFX}^2)$$

– Analyze per-study contrasts as “data”

based on Con’s + SE’s

• Fixed-Effects (FFX) GLM

$$\frac{1}{K} \sum_{k} \hat{\theta}_k \sim \mathcal{N}(0, \sum_{k} \sigma_{FFX,k}^2 / K^2)$$

– *Don’t* estimate variance, just take from first level

(Slide adapted from Thomas Nichols, OHBM 2015)
**Image-Based Meta-Analysis**

**In practice!**
- Not all of these options are easily used

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<th>Neuroimaging Implementation</th>
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<td>Con’s + SE’s</td>
<td>FSL’s FEAT</td>
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<td></td>
<td>SPM      spm_mfx</td>
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(Slide from Thomas Nichols, OHBM 2015)
Self Promotion Alert: IBMA toolbox

- SPM Extension
- Still in beta!
  - But welcome all feedback

- Available on GitHub

https://github.com/NeuroimagingMetaAnalysis/ibma
Meta-analysis of 21 pain studies

• Results
  – GLM methods similar
  – Z-based methods similar
  – But FFX Z methods more sensitive (as expected)

Fig. 1: Result of a meta-analysis of 21 pain studies for 4 fixed-effects (FFX GLM, Fisher, Stouffer, weighted-z) and 2 random-effects (RFX GLM, Stouffer MFX) meta-analytic approaches compared to the reference (MFX GLM) at a threshold of p<0.05 FDR corrected.

Data: Tracey pain group, FMRIB, Oxford.
Share image data supporting neuroimaging results
Share your statistic maps

http://neurovault.org
Share your statistic maps

http://neurovault.org
From SPM & FSL

$ nidmfsl fsl_ds107_group 49 -g Control

http://nidm.nidash.org/getting-started/
Conclusions

• When data available, **Image-Based** preferred to **Coordinate-Based** meta-analysis

For more on NIDM-Results
Maumet et al., Poster 1851 - Tuesday 12:45-14:45
“NIDM-Results: Standardized reporting of mass univariate neuroimaging results in SPM, FSL and AFNI”
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• Data sharing tools: **NeuroVault**, NIDM-Results

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Thank you!

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