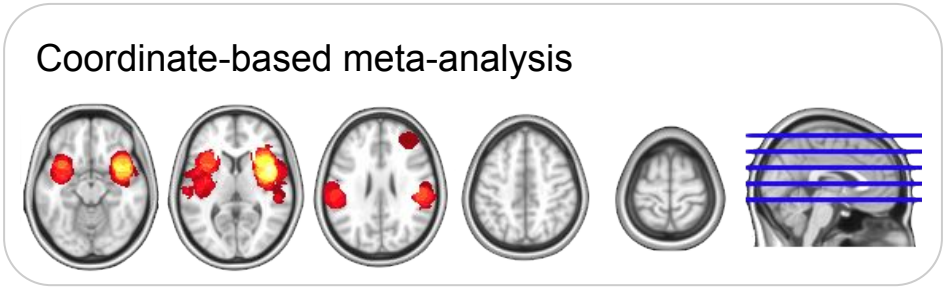
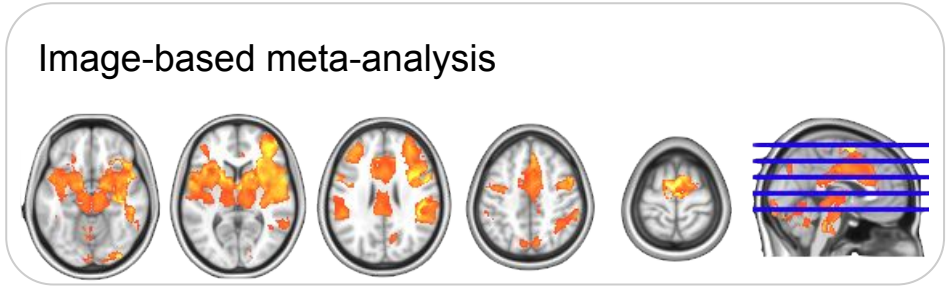
Practical intensity-based meta-analysis





Camille Maumet

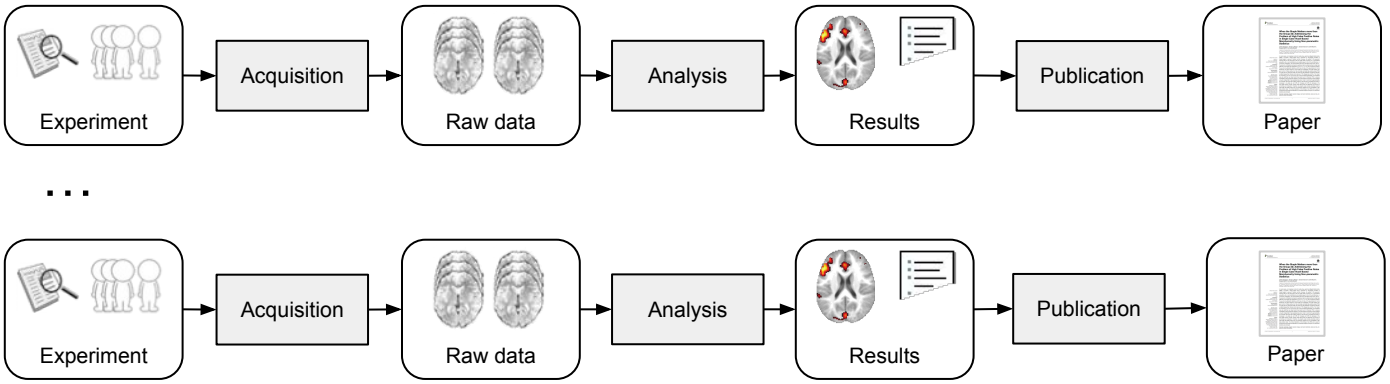
Presented by Thomas Nichols

OHBM Neuroimaging Meta-Analysis Educational course

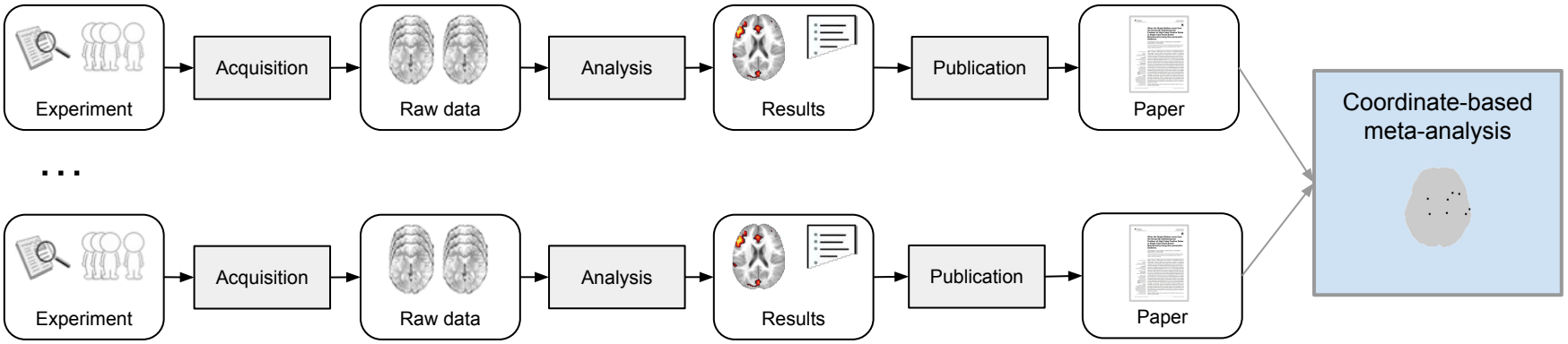
June 17th 2018

Coordinate-Based & Image-Based Meta-Analyses

Neuroimaging meta-analyses

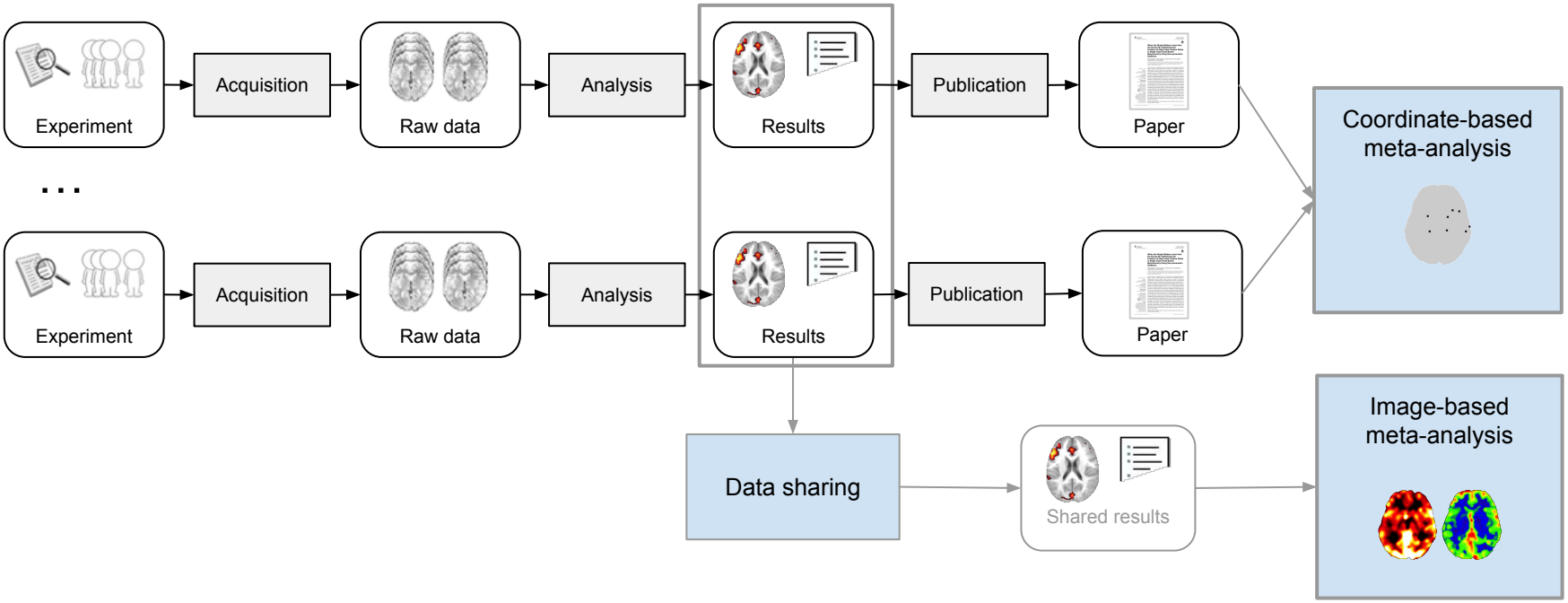


Neuroimaging meta-analyses



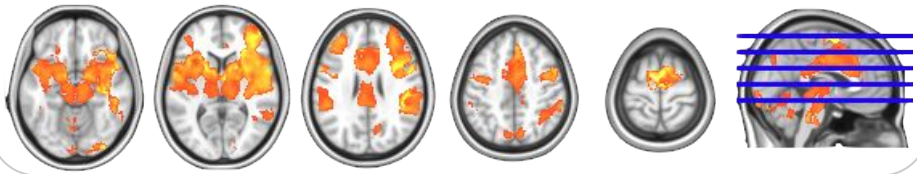
Coordinate-based meta-analysis

Neuroimaging meta-analyses



Coordinate-based meta-analysis

Image-based meta-analysis



How to perform an image-based meta-analysis?

Image-based meta-analysis

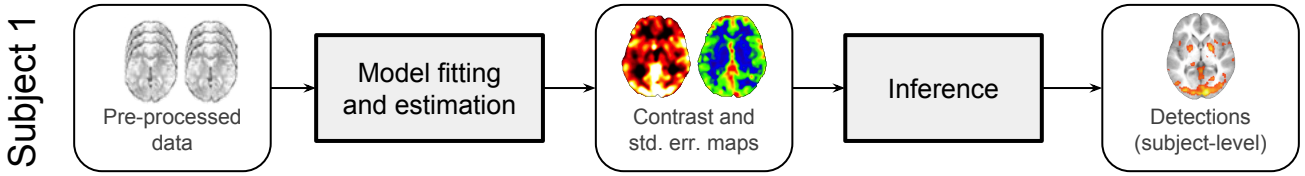


Image-based meta-analysis

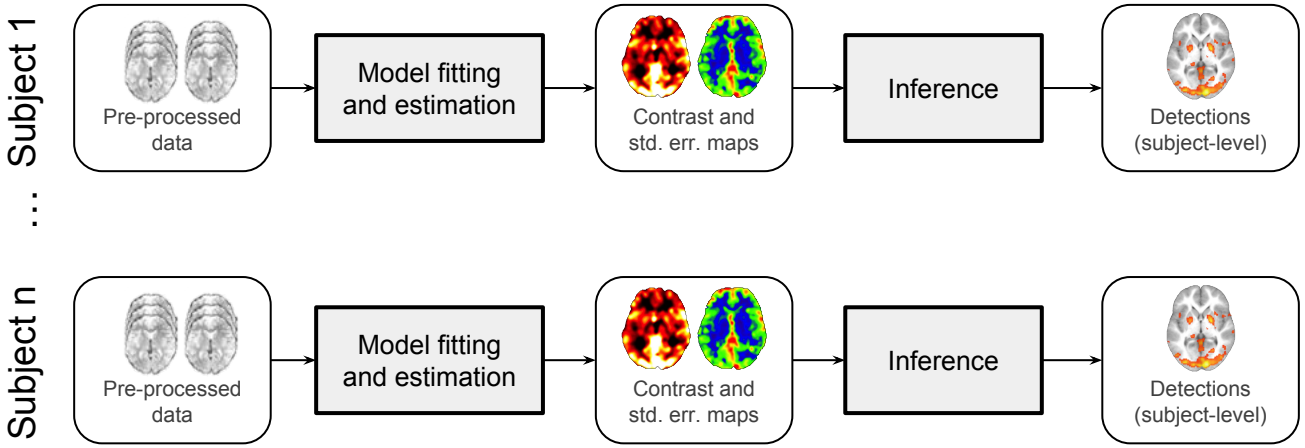


Image-based meta-analysis

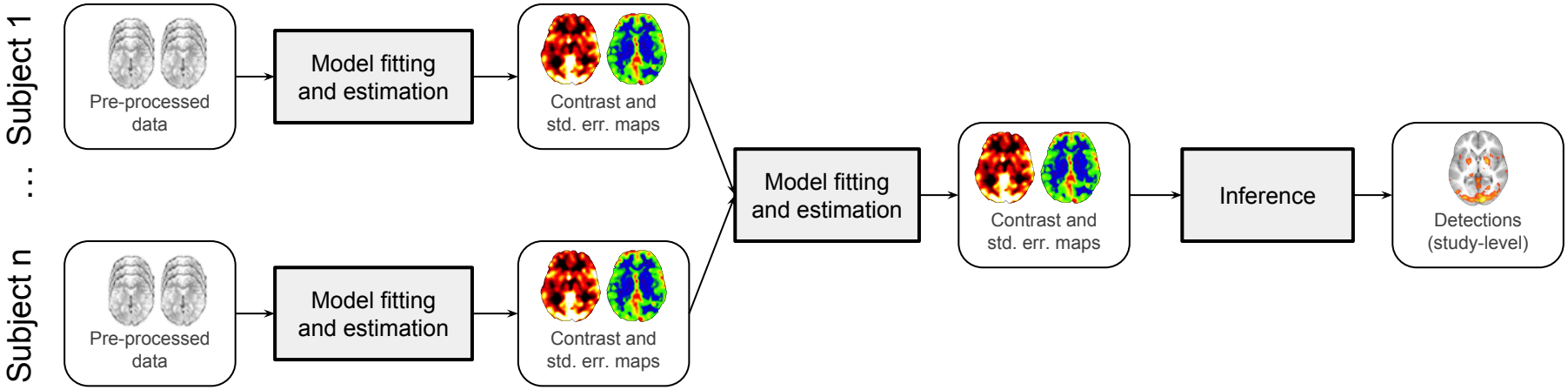


Image-based meta-analysis

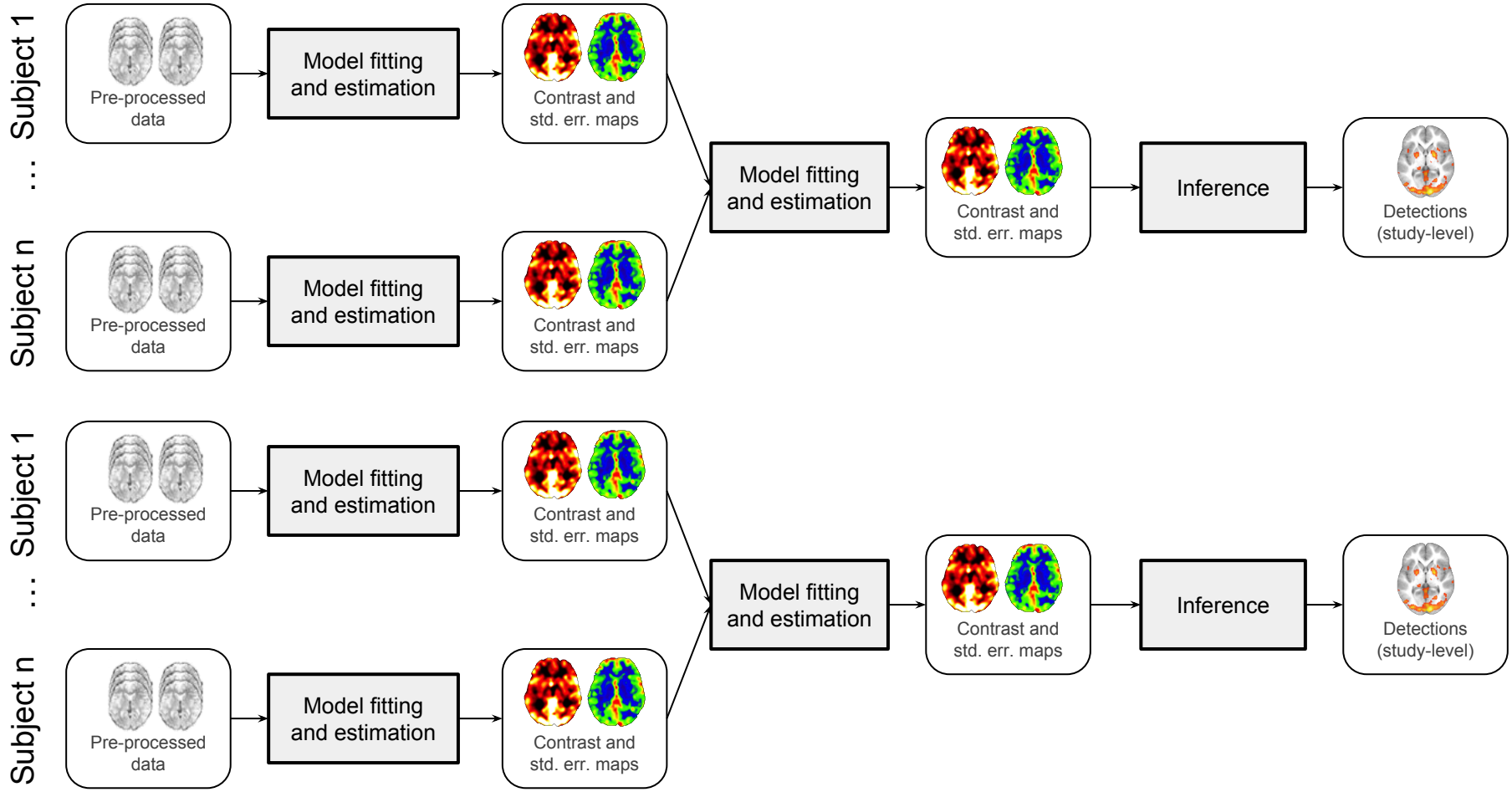


Image-based meta-analysis

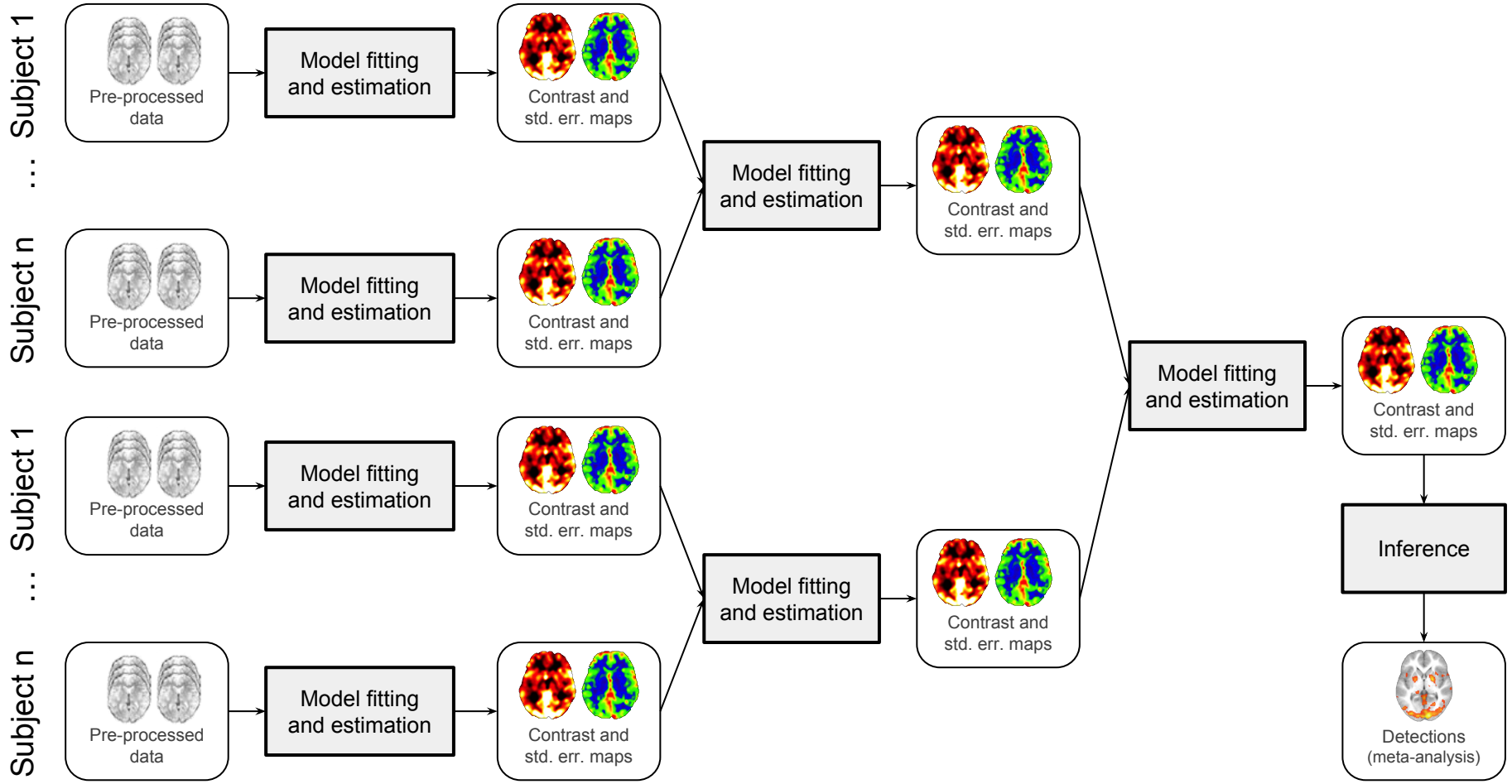


Image-based meta-analysis

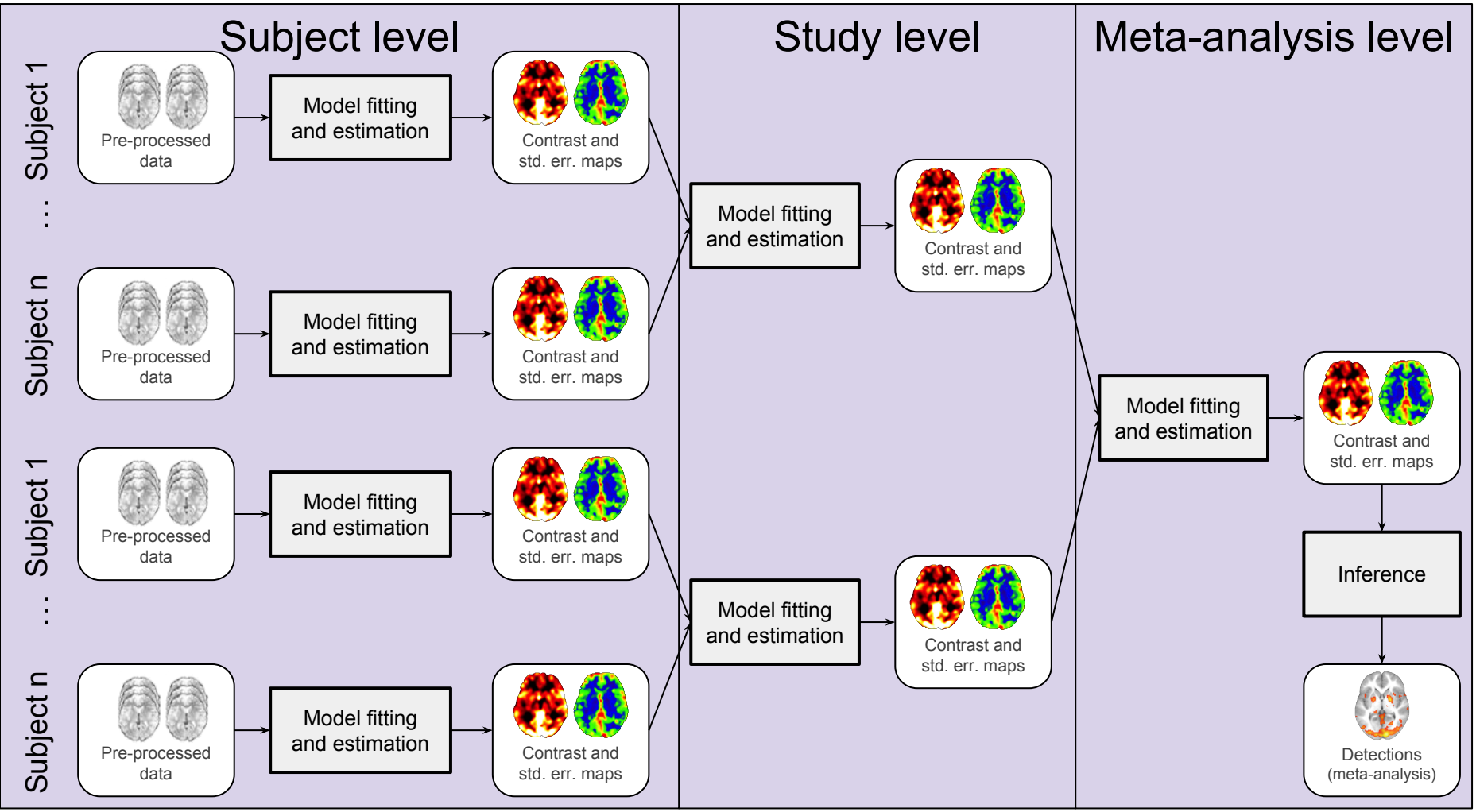
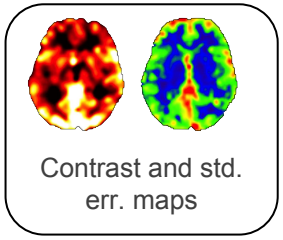


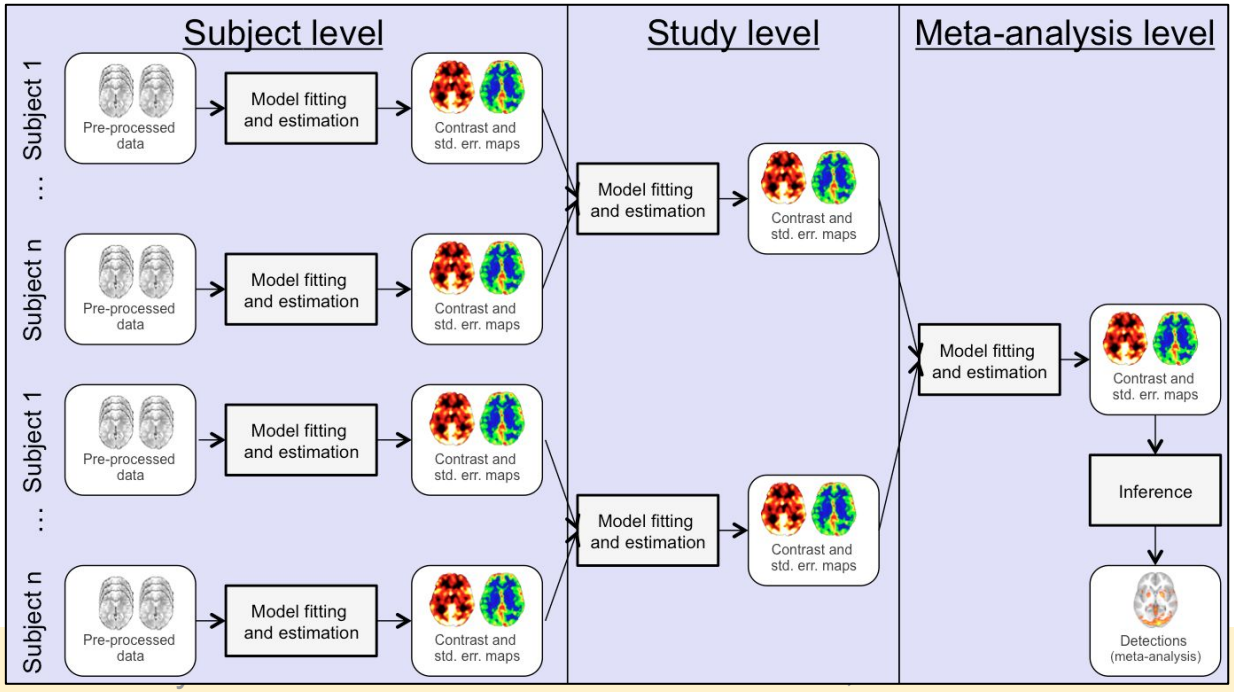
Image-based meta-analysis



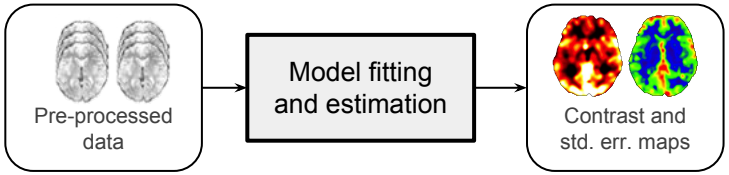
- Gold standard:

  Third-level Mixed-Effects GLM

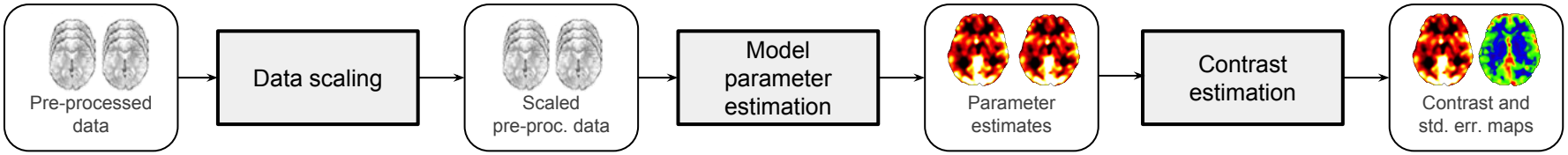
- Requirements
  - study-level **Contrast estimates** and **Standard error** maps.
  - Same **units**



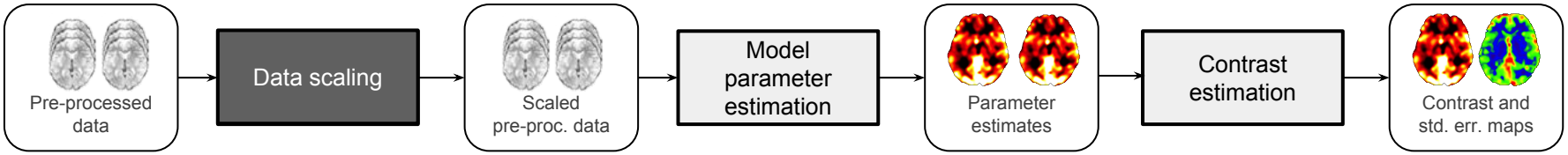
Units of contrast estimates



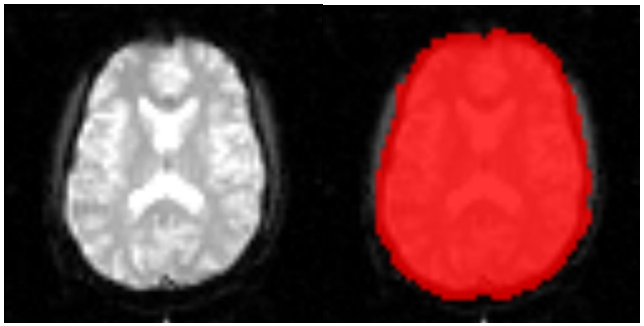
Units of contrast estimates



Units of contrast estimates

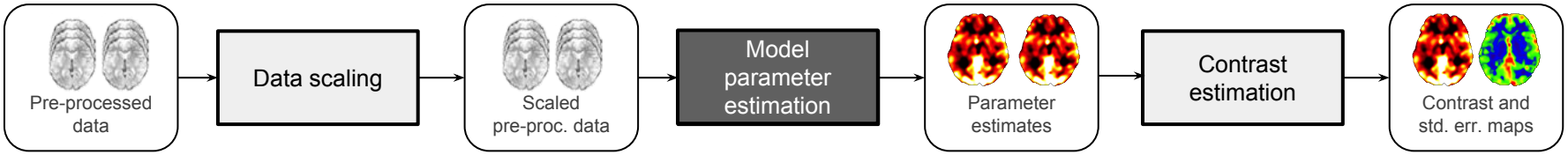


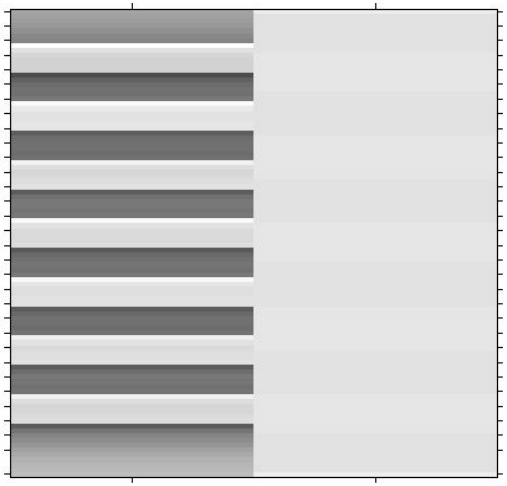
$$\text{scaled\_data} = \frac{\text{data} * \text{target}}{\text{est\_mean}}$$



Units depend on **mean estimation** and **scaling target**.

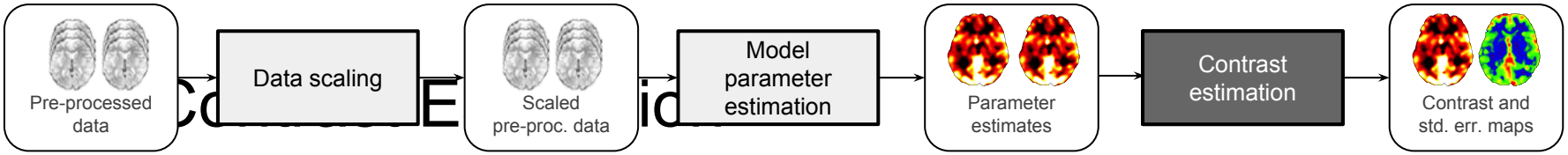
Units of contrast estimates



$Y =$  $\beta + \varepsilon$

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

Units of contrast estimates

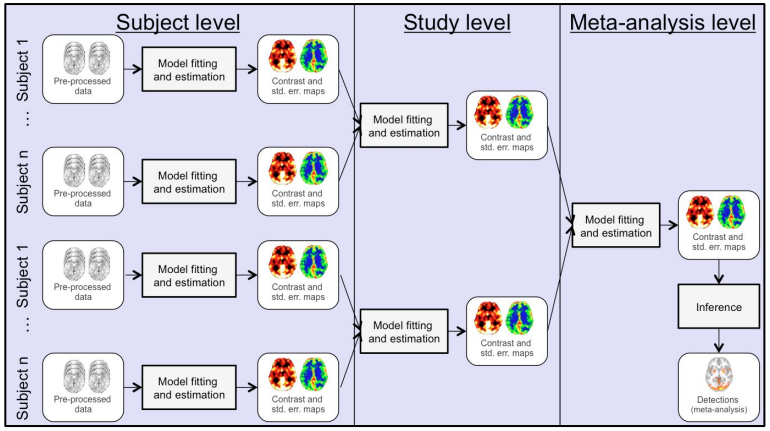


- Linear combination of parameter estimates
- Final statistics invariant to scale
  - e.g. [1 1 1 1] gives same T's & P's as [¼ ¼ ¼ ¼]

Units depend on **contrast vector**

- Rule for contrasts to preserve units
  - Positive elements sum to 1
  - Negative elements sum to -1

Units of contrast estimates

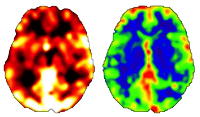
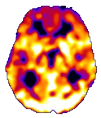
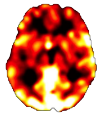


- Gold standard:

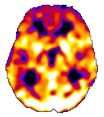
Third-level Mixed-Effects GLM

- 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	FSL	AFNI
 **Contrast** & **std. err.** maps	con_0001.nii [SPM.mat]	cope1.nii varcope1.nii (*squared*)	3dMEMA_result+tlrc.BRIK[[0]] [from contrast & stat maps]
 **Statistic** map E.g. Z-map	spmT_0001.nii	tstat1.nii.gz zstat1.nii.gz	3dMEMA_result+tlrc.BRIK[[1]]
 **Contrast** map	con_0001.nii	cope1.nii	3dMEMA_result+tlrc.BRIK[[0]]

IBMA on Z maps



Statistic map
E.g. Z-map

- 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)

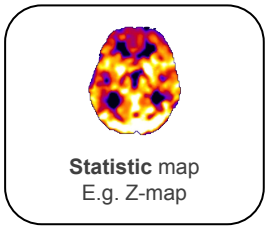
- "Stouffer's Random Effects (RFX)"

$$\sqrt{K} \times \frac{1}{K}\sum_k Z_k \sim \mathcal{N}(0,\sigma^2_{RFX})$$

  - Submit Z's to one-sample t-test

(Slide adapted from Thomas Nichols, OHBM 2015)

IBMA on Z maps + N



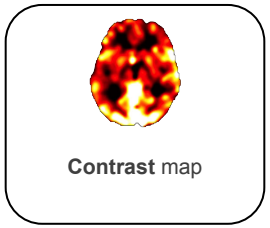
- Weighted Stouffer's

$$\sum_k w_k Z_k \sim \mathcal{N}(0,1), \quad w_k \propto \sqrt{N_k}$$

  - Z's from bigger studies get bigger weights

(Slide adapted from Thomas Nichols, OHBM 2015)

IBMA on Contrast maps

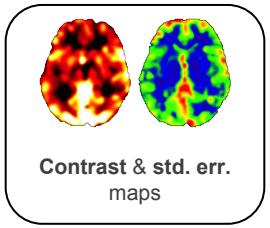


- Random Effects (RFX) GLM

$$\frac{1}{K}\sum_k c\hat{\beta}_k \sim \mathcal{N}(0, \sigma^2_{\mathrm{RFX}})$$

  - Analyze per-study contrasts as “data”

Contrast + standard error maps



- Fixed-Effects (FFX) GLM

$$\frac{1}{K}\sum_k \hat{\theta}_k \sim \mathcal{N}(0, \sum_k \sigma^2_{\mathrm{FFX},k}/K^2)$$

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

(Slide adapted from Thomas Nichols, OHBM 2015)

Implementations

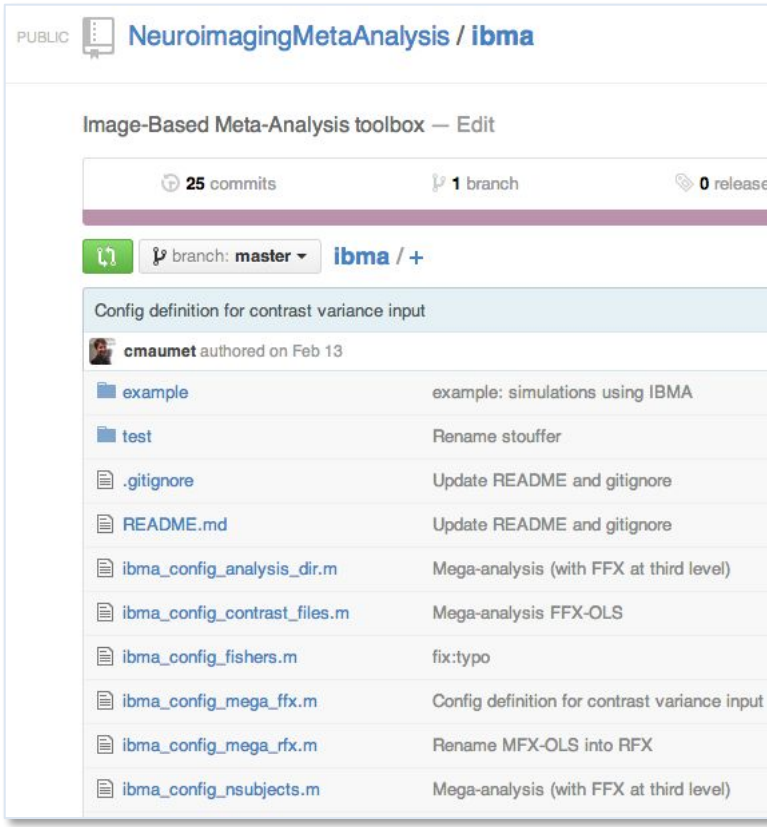
- Not all of these options are easily used

Meta-Analysis Method	Inputs	Neuroimaging Implementation
'Gold Standard' MFX	Con's + SE's	FSL's `FEAT` SPM `spm_mfx` AFNI `3dMEMA`
RFX GLM Stouffer's RFX	Con's Z's	FSL, SPM, AFNI, etc…
FFX GLM Fisher's Stouffer's Stouffer's Weighted	Con's +SE's Z's Z's Z's + N's	n/a

(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)

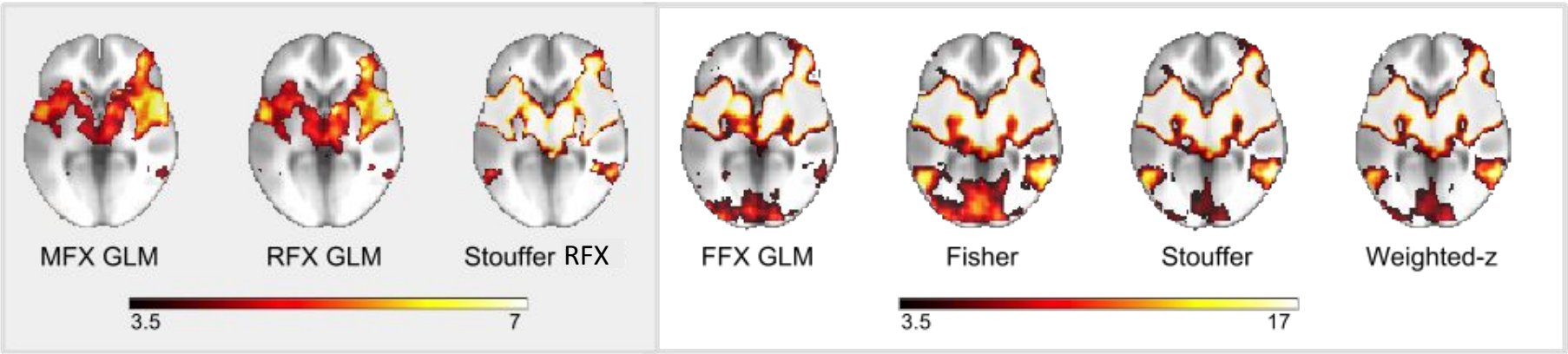
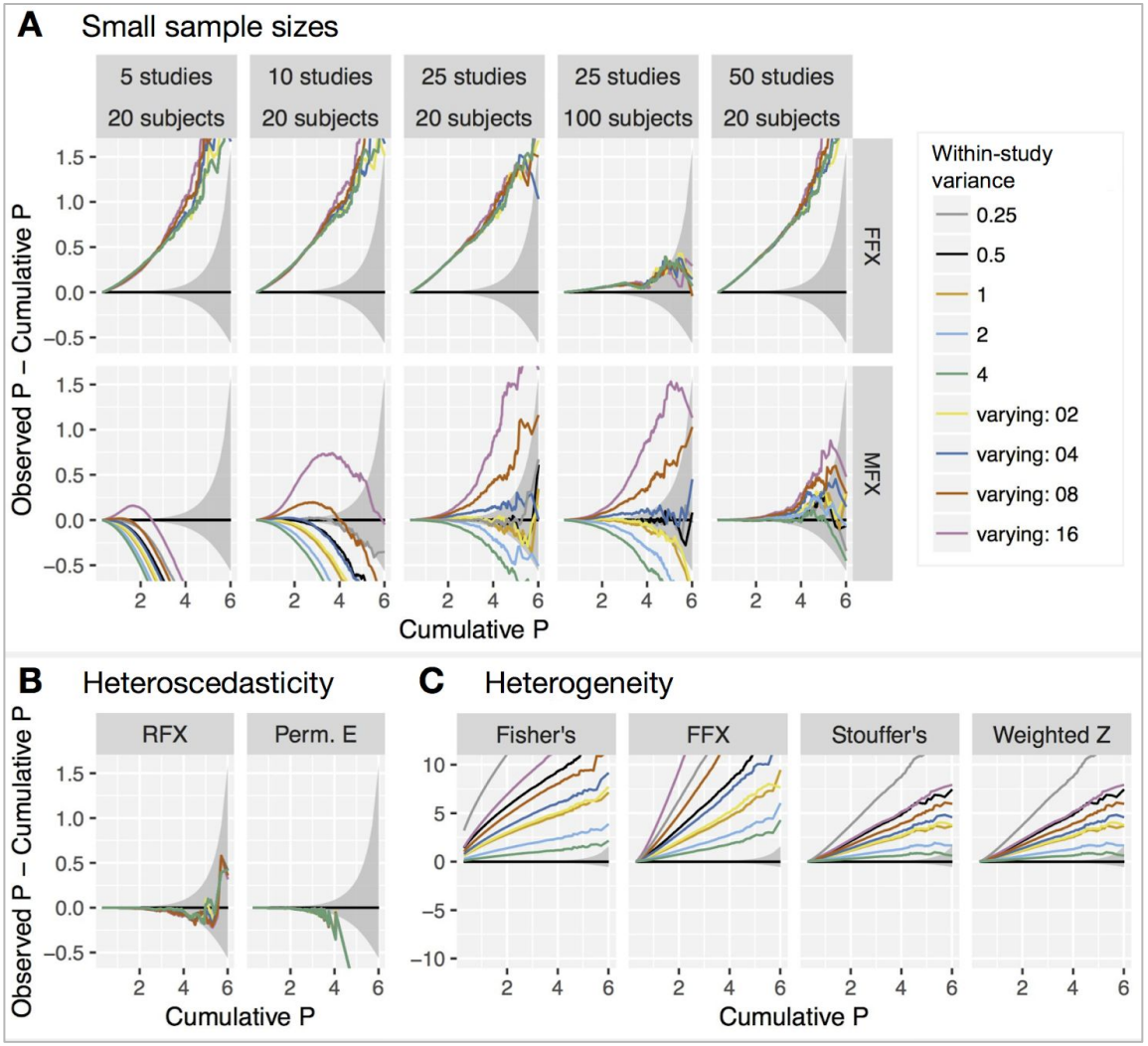


Fig. 1: Result of a meta-analysis of 21 pain studies for 4 fixed-effects (FFX GLM, Fisher, Stouffer, weighted-z) and 2 random-effects (RFX GLM, Stouffer MFX) meta-analytic approaches compared to the reference (MFX GLM) at a threshold of $p<0.05$ FDR corrected.

Data: Tracey pain group, FMRIB, Oxford.

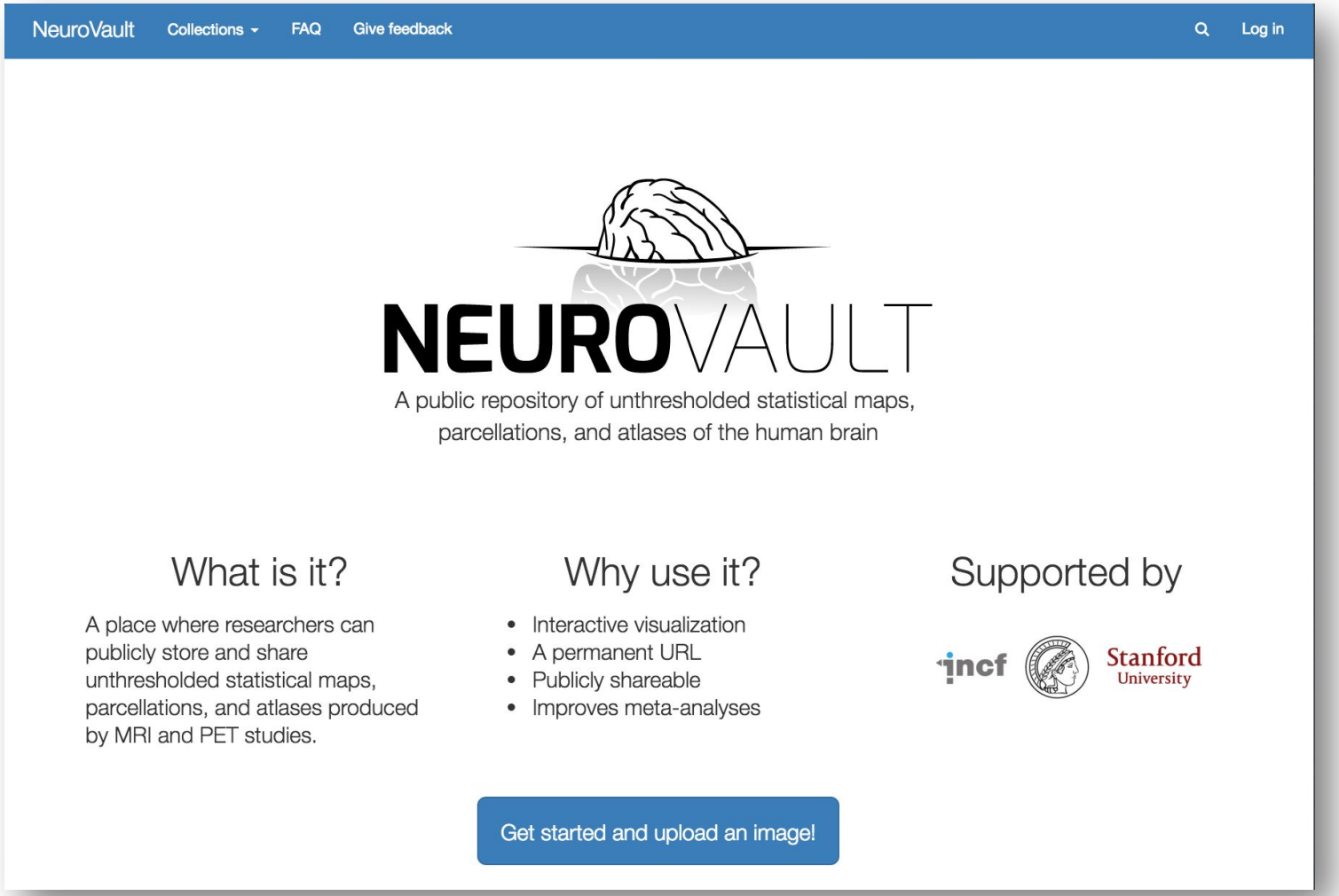
Self Promotion Alert: Robustness of the meta−analytic estimators

Poster 2653



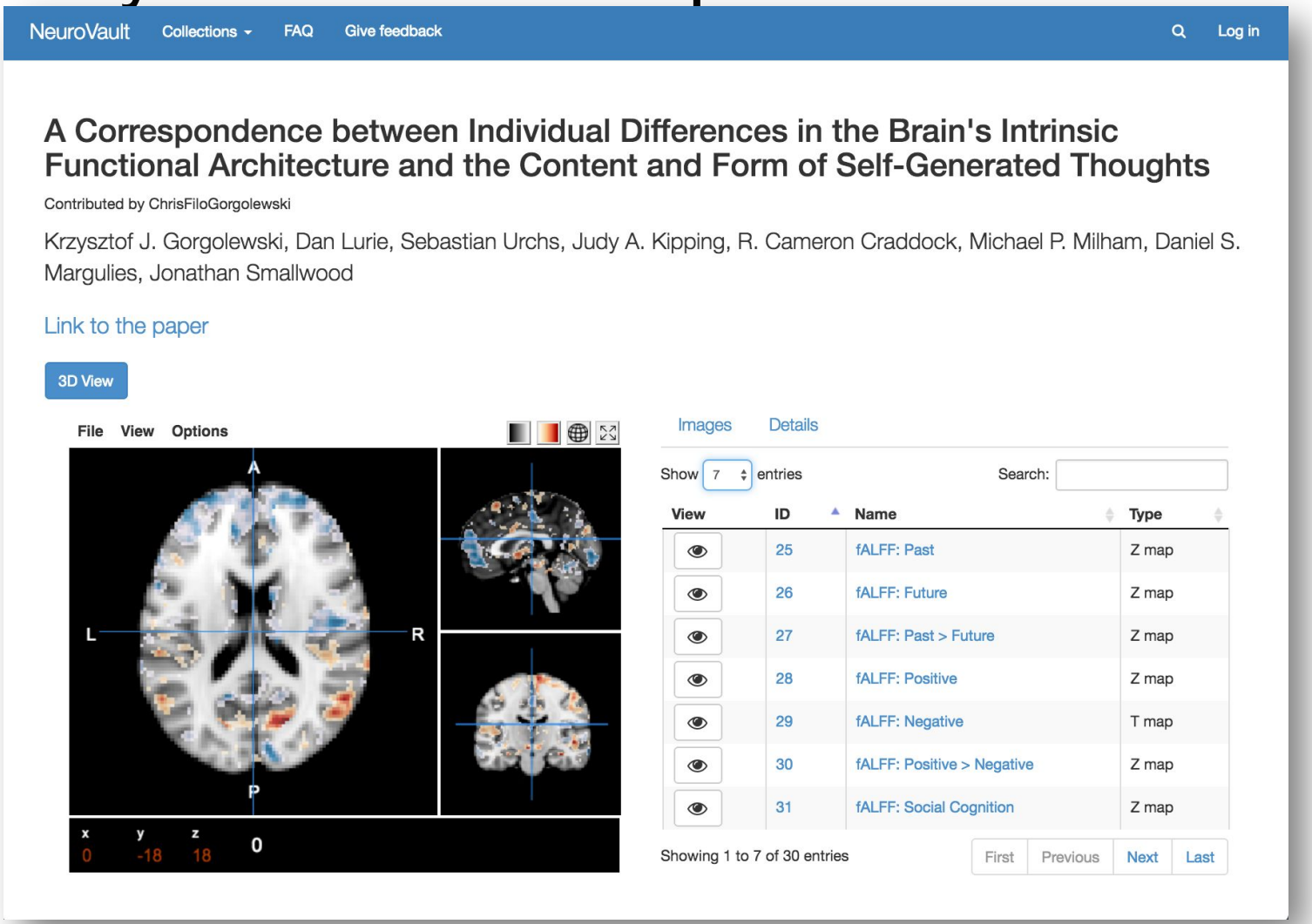
How to publish your statistic maps?

Share your statistic maps



http://neurovault.org

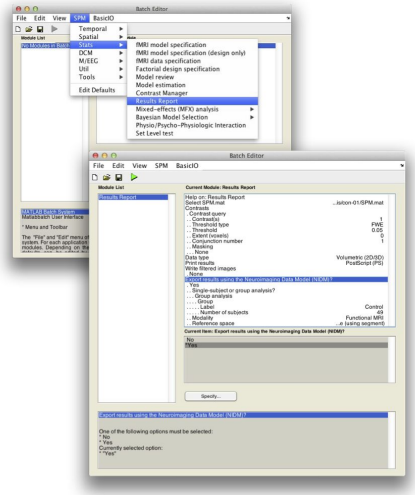
Share your statistic maps

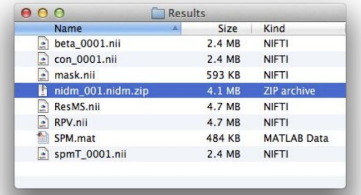


http://neurovault.org

From SPM & FSL

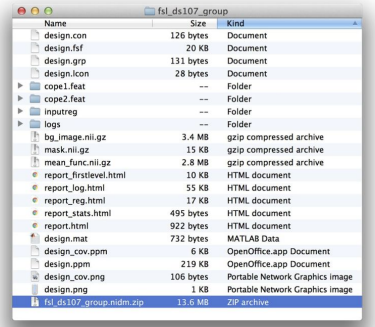
SPM

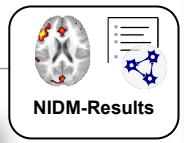




FSL

```
$ nidmfsl fsl_ds107_group 49 -g Control
```





NEUROVAULT

A public repository of unthresholded statistical maps, parcellations, and atlases of the human brain

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

Conclusions

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

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- Few tools for Z-based IBMA, but underway…

Conclusions

- When data available, **Image-Based** preferred to **Coordinate-Based** meta-analysis
- **In practice**, it is **difficult** to use the gold standard **Mixed-Effects GLM**
- When only contrast estimates are available, **RFX GLM** is a practical & valid approach
- Few tools for Z-based IBMA, but underway…
- Data sharing tools: **NeuroVault**, NIDM-Results

Thank you!

This work is supported by