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## Practical Intensity Based Meta-Analysis

Camille Maumet, Thomas E. Nichols

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Submitted on 7 May 2023

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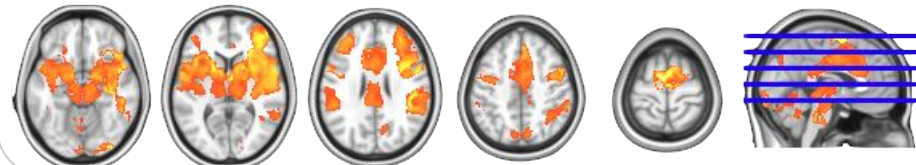
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# Practical intensity-based meta-analysis

Coordinate-based meta-analysis



Image-based meta-analysis



Camille Maumet

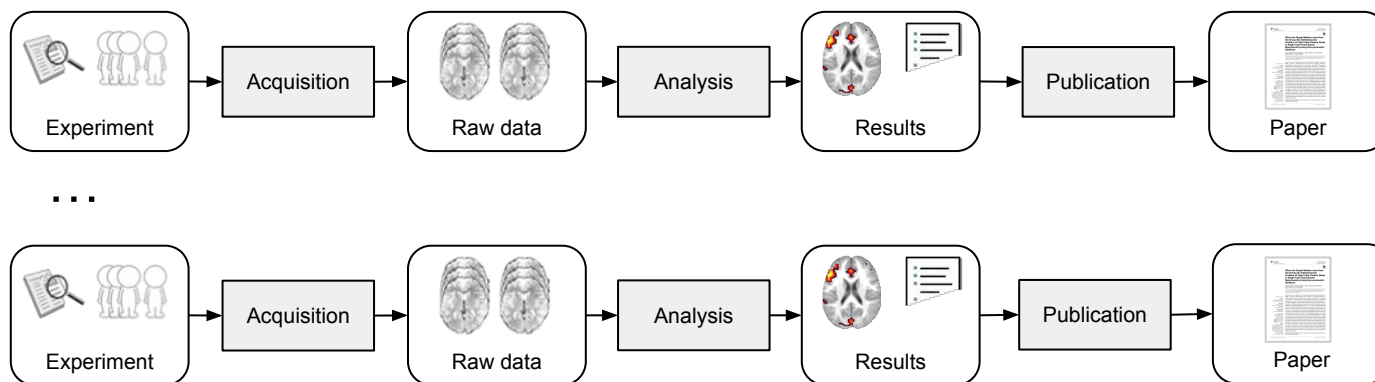
Presented by Thomas Nichols

OHBM Neuroimaging Meta-Analysis Educational course

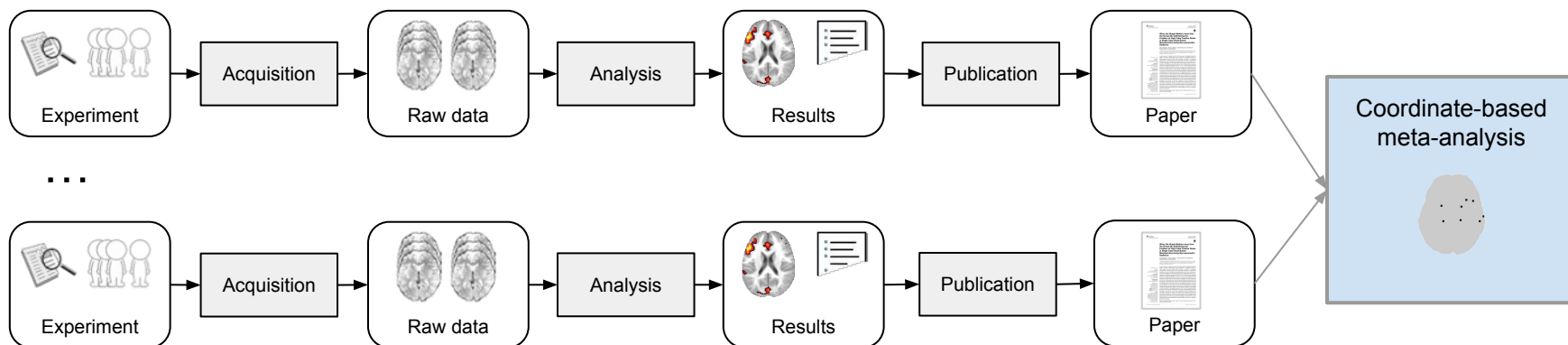
June 17<sup>th</sup> 2018

# Coordinate-Based & Image-Based Meta-Analyses

# Neuroimaging meta-analyses



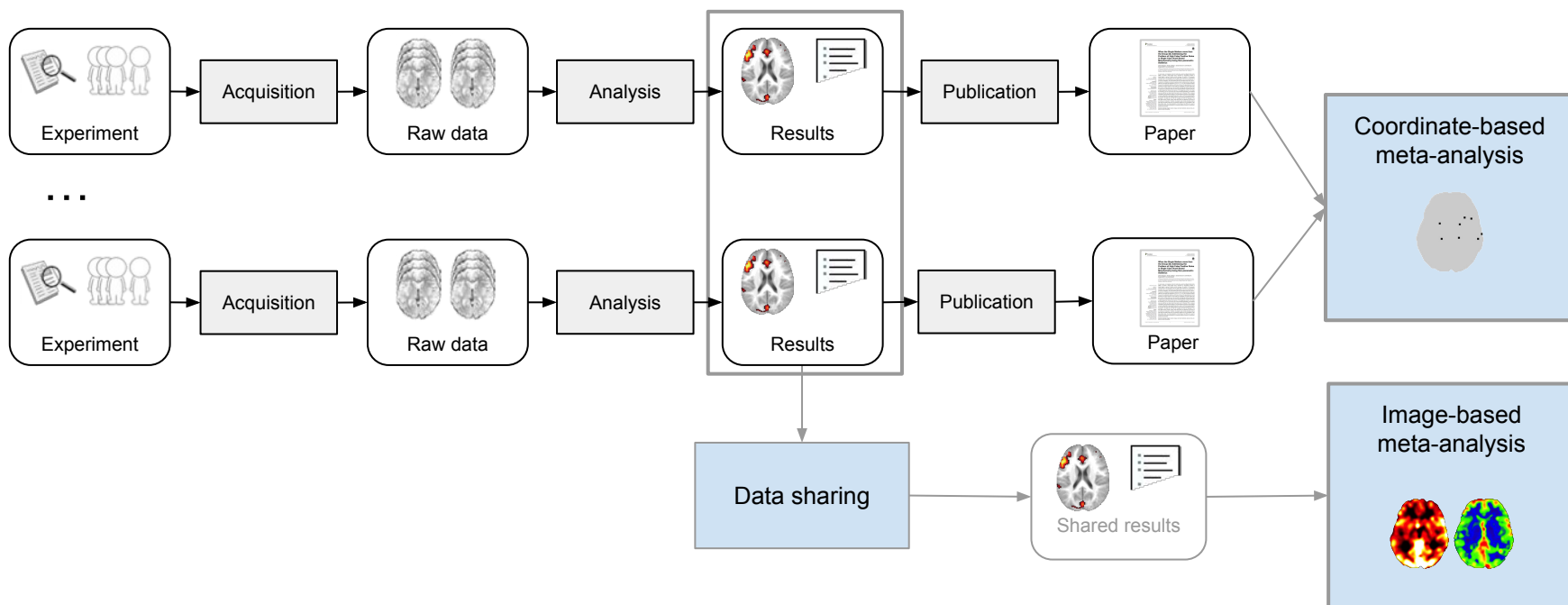
# Neuroimaging meta-analyses



## Coordinate-based meta-analysis



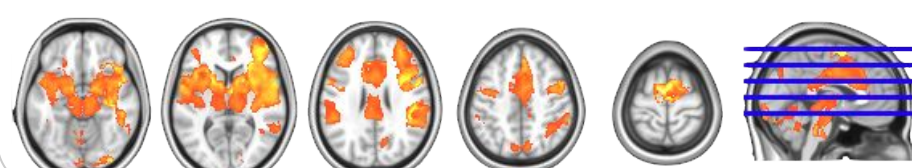
# Neuroimaging meta-analyses



Coordinate-based meta-analysis



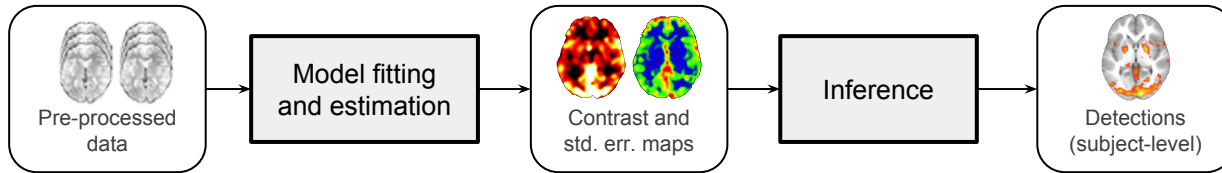
Image-based meta-analysis



How to perform an image-based  
meta-analysis?

# Image-based meta-analysis

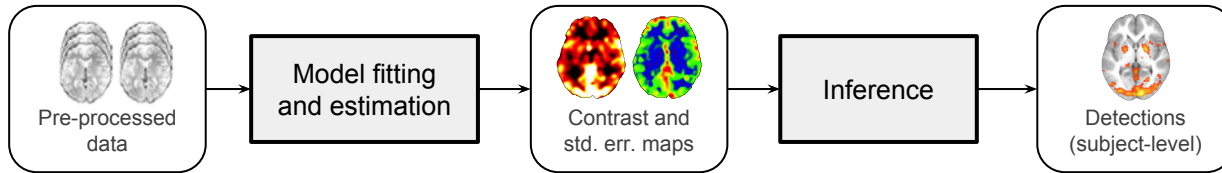
Subject 1



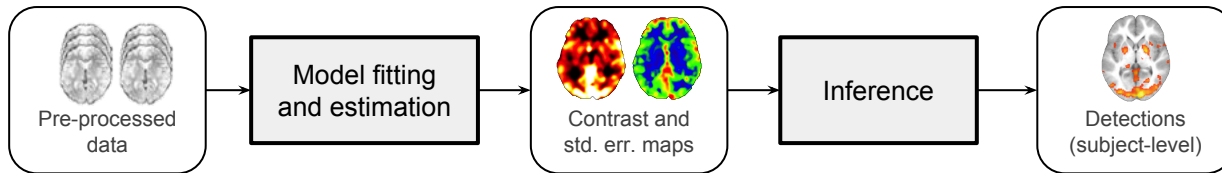


# Image-based meta-analysis

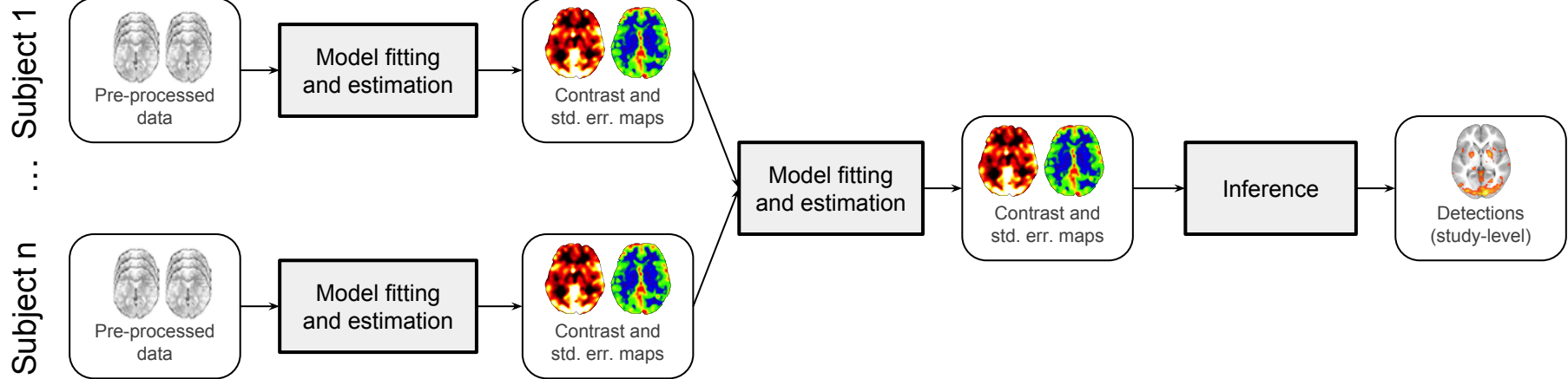
Subject 1  
...



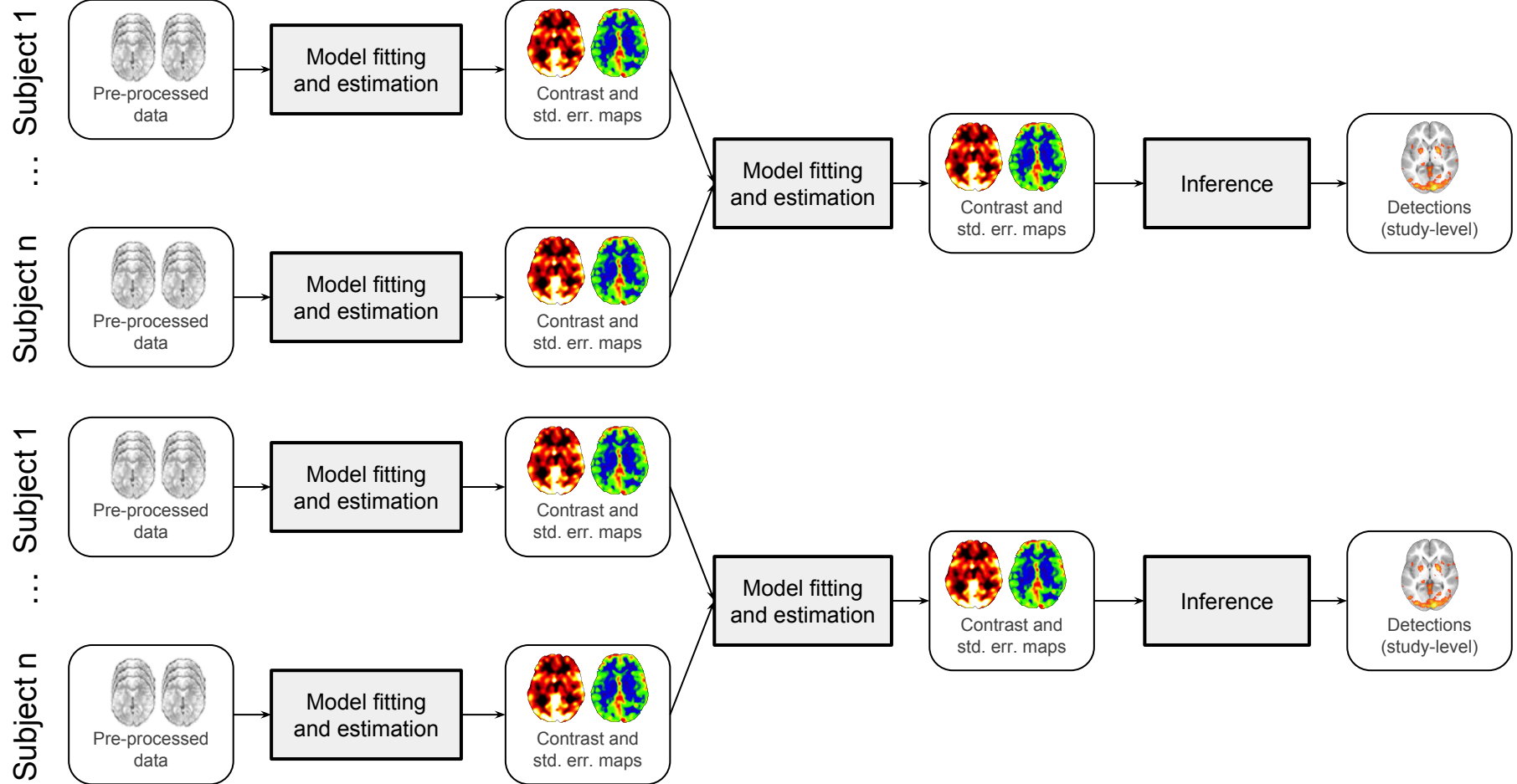
Subject n



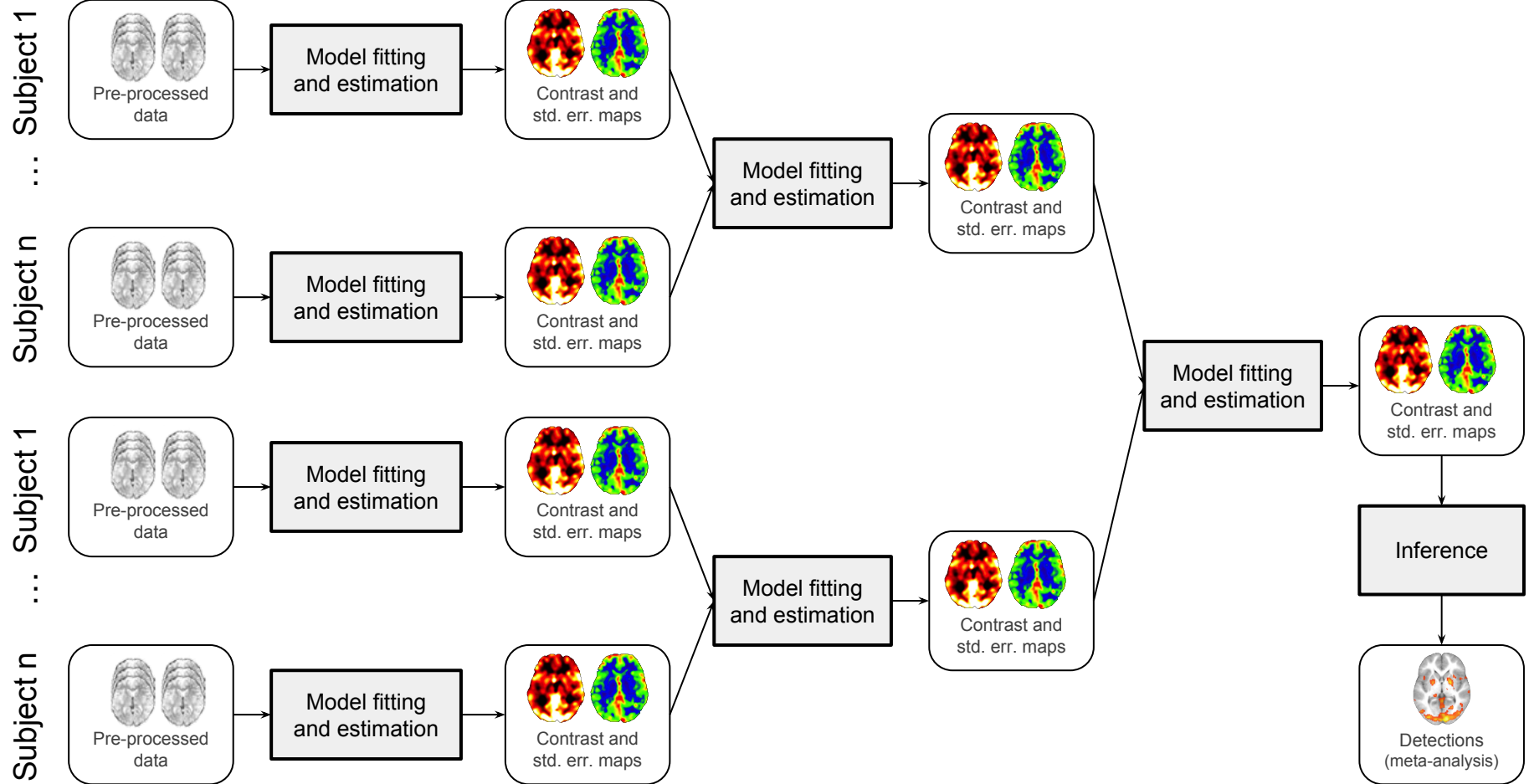
# Image-based meta-analysis



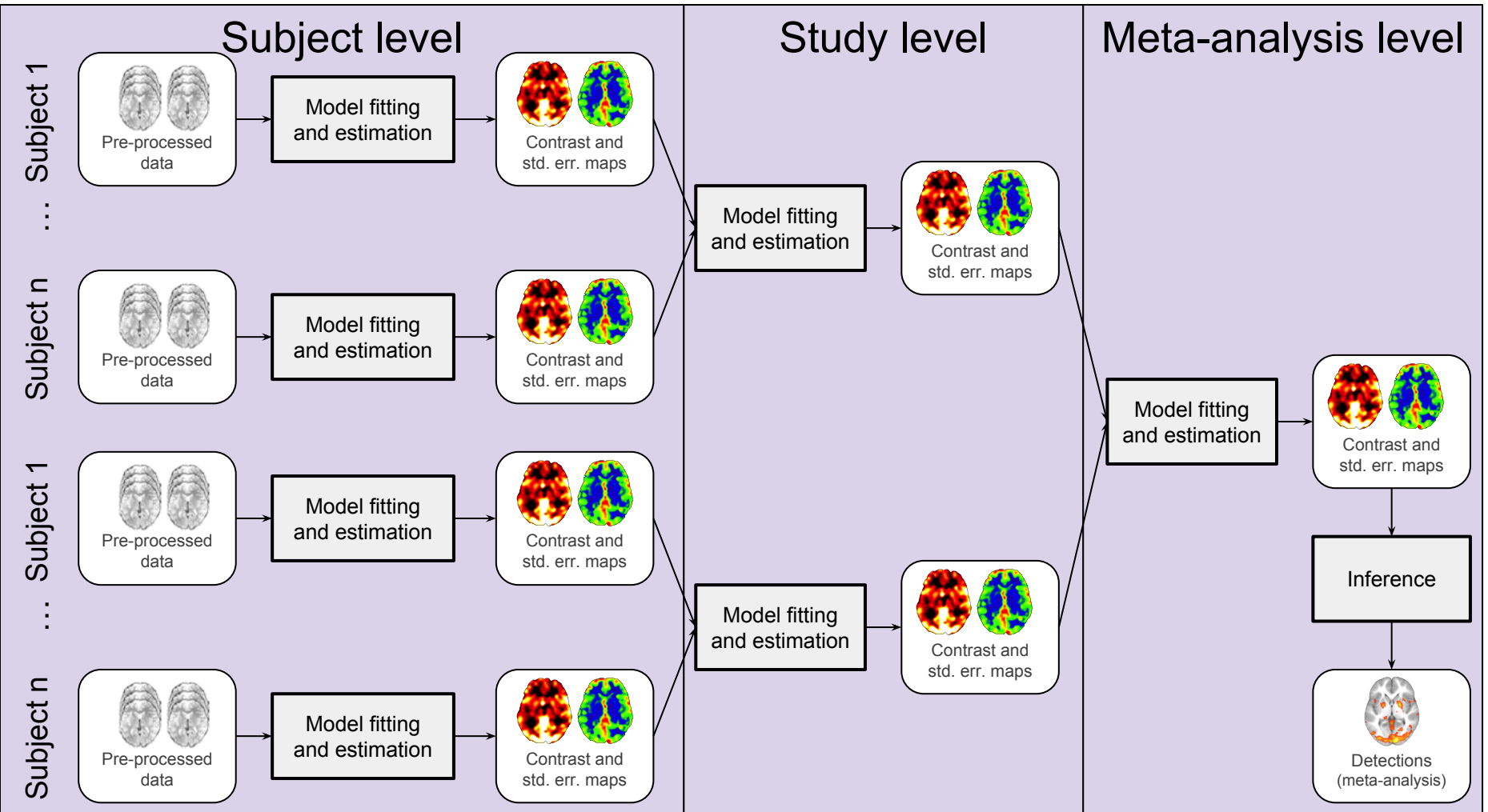
# Image-based meta-analysis



# Image-based meta-analysis



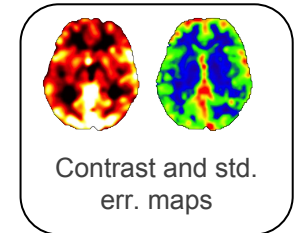
# Image-based meta-analysis



# Image-based meta-analysis

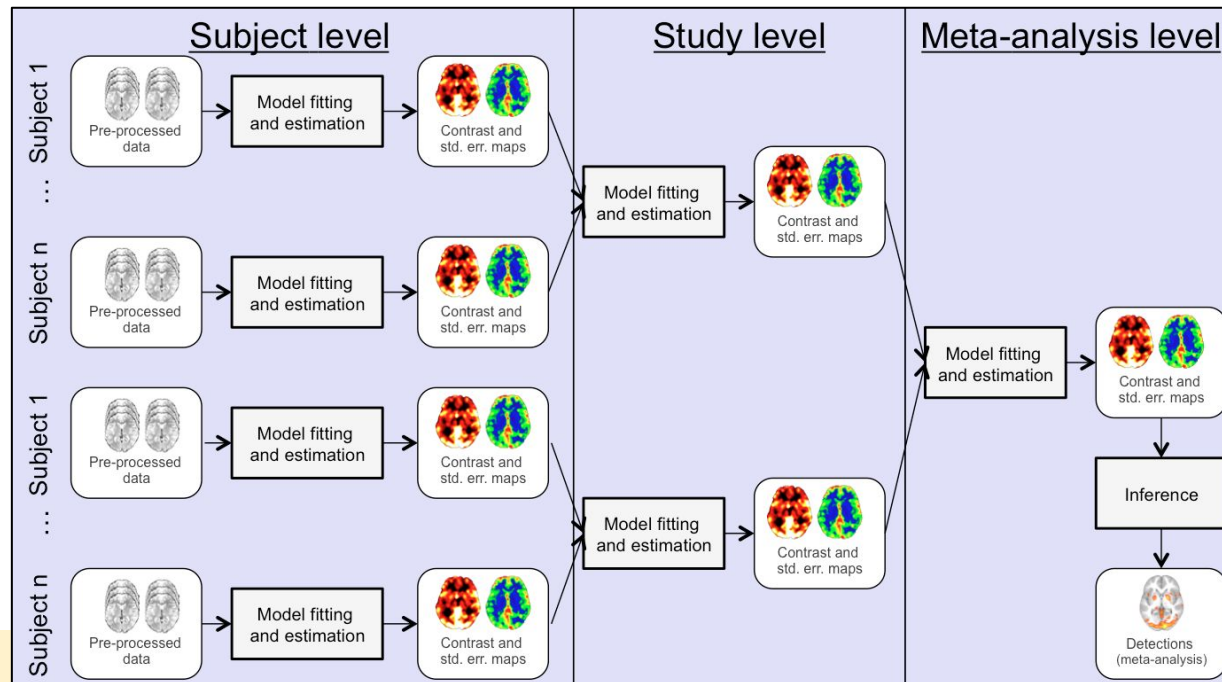
- Gold standard:

## Third-level Mixed-Effects GLM

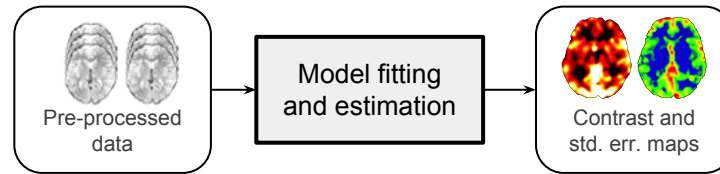


- Requirements

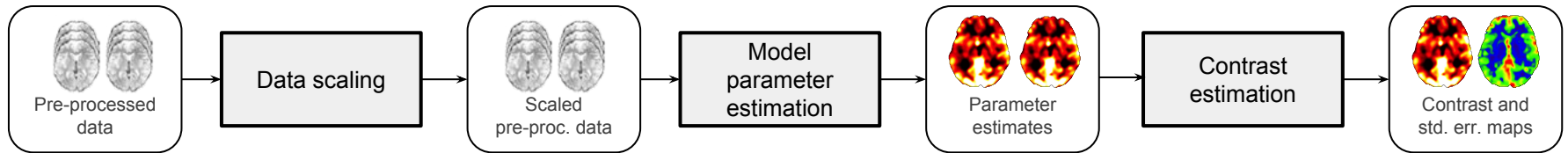
- study-level **Contrast estimates** and **Standard error maps.**
- **Same units**



# Units of contrast estimates

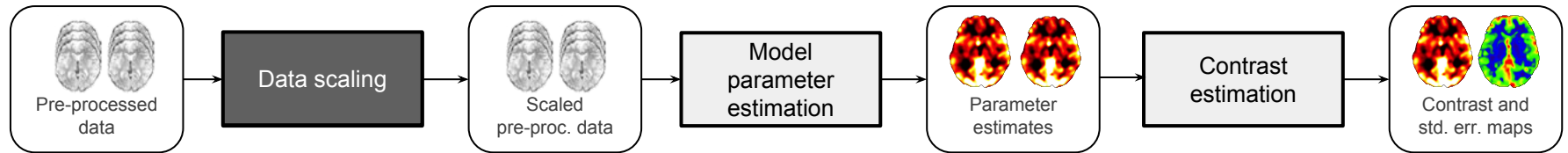


# Units of contrast estimates

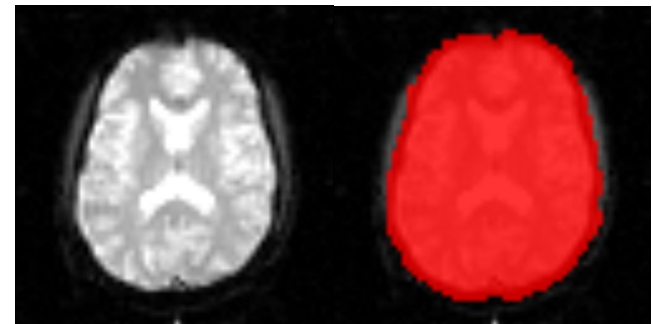




# Units of contrast estimates

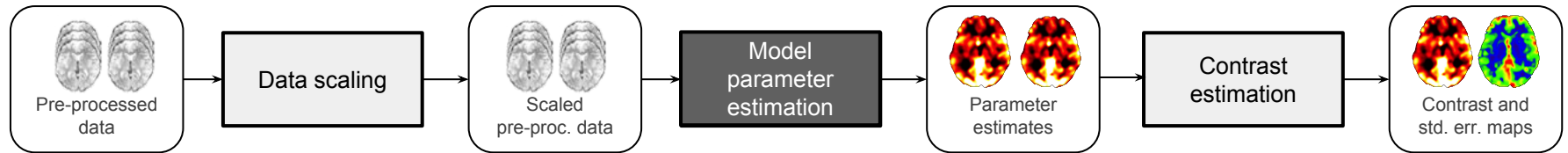


$$\text{scaled\_data} = \frac{\text{data} * \text{target}}{\text{est\_mean}}$$



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

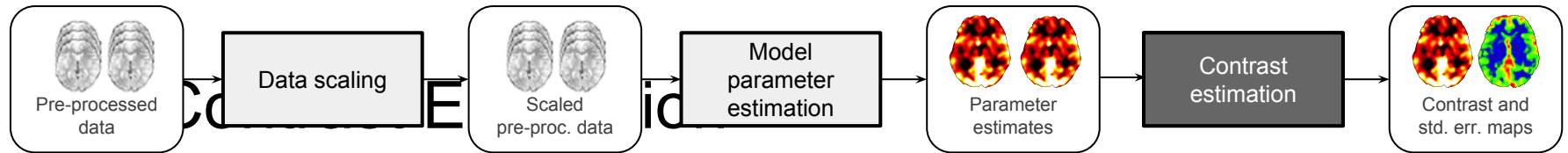
# Units of contrast estimates



$$Y = \begin{matrix} \text{[Matrix of data points]} \end{matrix} \beta + \epsilon$$

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  $[\frac{1}{4} \ \frac{1}{4} \ \frac{1}{4} \ \frac{1}{4}]$

## Units depend on **contrast vector**

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

# Units of contrast estimates

- Gold standard:

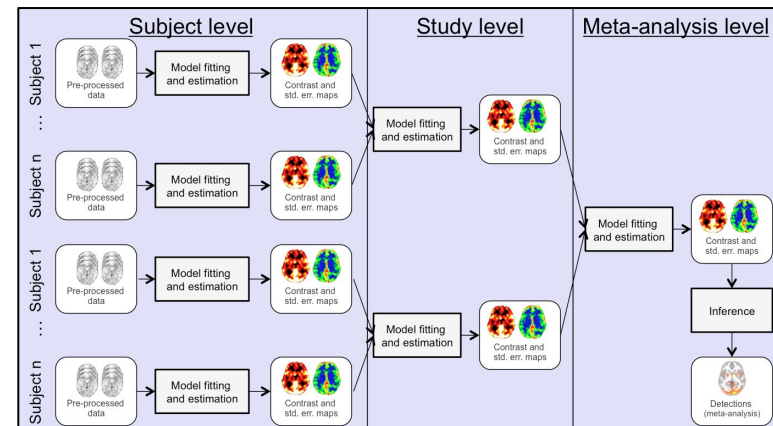
## Third-level Mixed-Effects GLM

- But...

– Units will depend on:

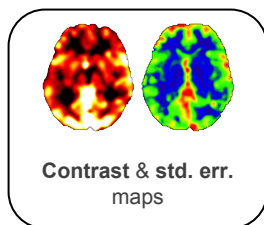
- The scaling of the data (subject-level)
- The scaling of the predictor(s) (subject- and study-level)
- The scaling of the contrast (subject- and study-level).

– Contrast estimates and standard error maps are rarely shared...



# Which images for IBMA?

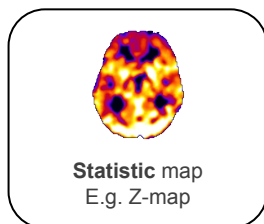
SPM



con\_0001.nii  
[SPM.mat]

cope1.nii  
varcope1.nii (*squared*)

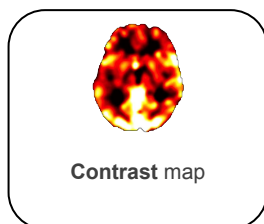
3dMEMA\_result+tlrc.BRIK[[0]]  
[from contrast & stat maps]



spmT\_0001.nii

tstat1.nii.gz  
zstat1.nii.gz

3dMEMA\_result+tlrc.BRIK[[1]]

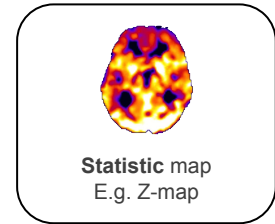


con\_0001.nii

cope1.nii

3dMEMA\_result+tlrc.BRIK[[0]]

# IBMA on Z maps



- Fisher's

$$-2 \sum_k \log P_k \sim \chi_{2k}^2$$

- 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  $\mathcal{N}(0,1)$

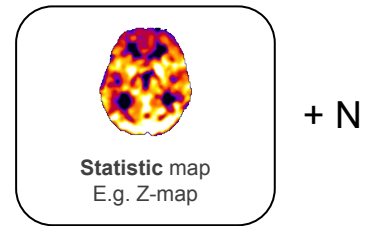
- “Stouffer's Random Effects (RFX)”

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

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

(Slide adapted from Thomas Nichols, OHBM 2015)

# IBMA on Z maps + N



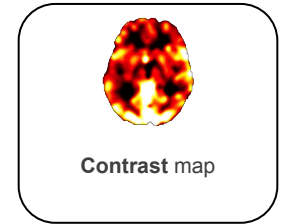
- Weighted Stouffer's

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

- Z's from bigger studies get bigger weights

(Slide adapted from Thomas Nichols, OHBM 2015)

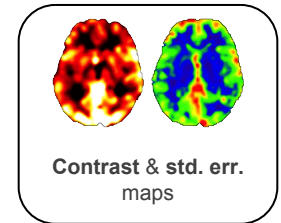
# IBMA on Contrast maps



- Random Effects (RFX) GLM

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

- Analyze per-study contrasts as “data”



## Contrast + standard error maps

- Fixed-Effects (FFX) GLM

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

- *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

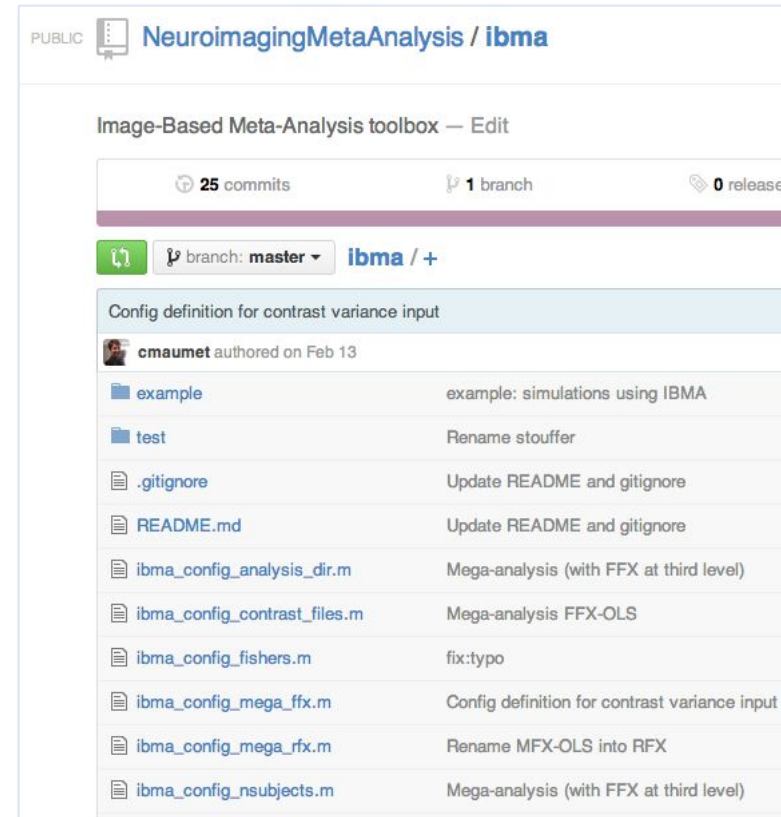
Meta-Analysis Method	Inputs	Neuroimaging Implementation
'Gold Standard' MFX	Con's + SE's	FSL's FEAT SPM spm_mfx AFNI 3dMEMA
RFX GLM Stouffer's RFX	Con's Z's	FSL, SPM, AFNI, etc...
FFX GLM Fisher's Stouffer's Stouffer's Weighted	Con's +SE's Z's Z's Z's + N's	n/a

(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)

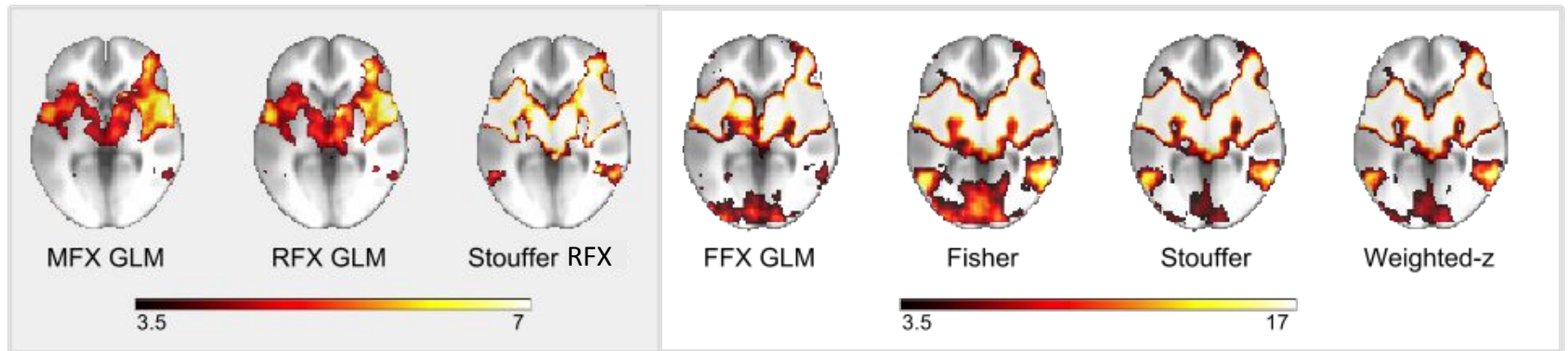
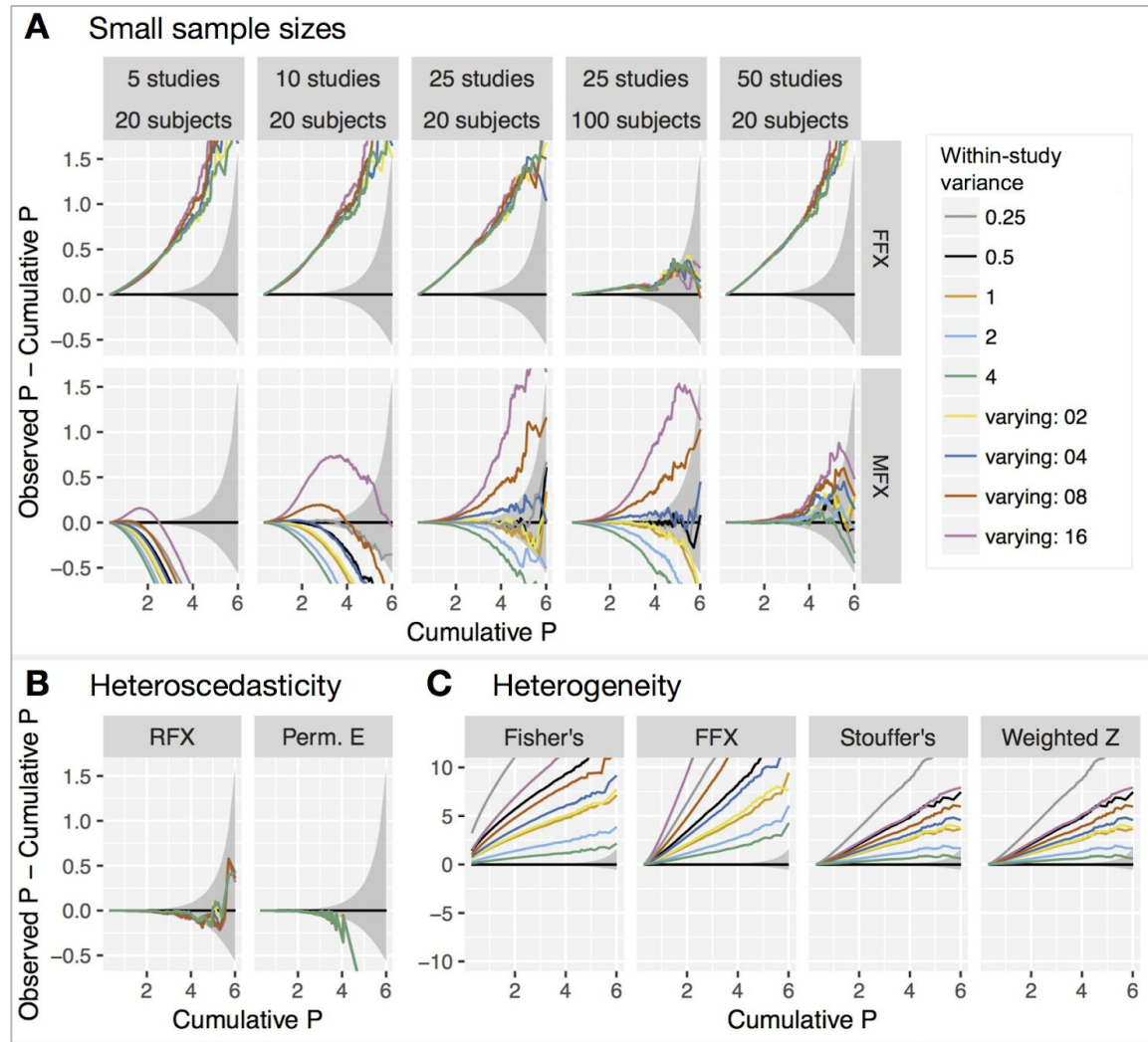


Fig. 1: Result of a meta-analysis of 21 pain studies for 4 fixed-effects (FFX GLM, Fisher, Stouffer, weighted-z) and 2 random-effects (RFX GLM, Stouffer MFX) meta-analytic approaches compared to the reference (MFX GLM) at a threshold of  $p < 0.05$  FDR corrected.

Data: Tracey pain group, FMRI, Oxford.

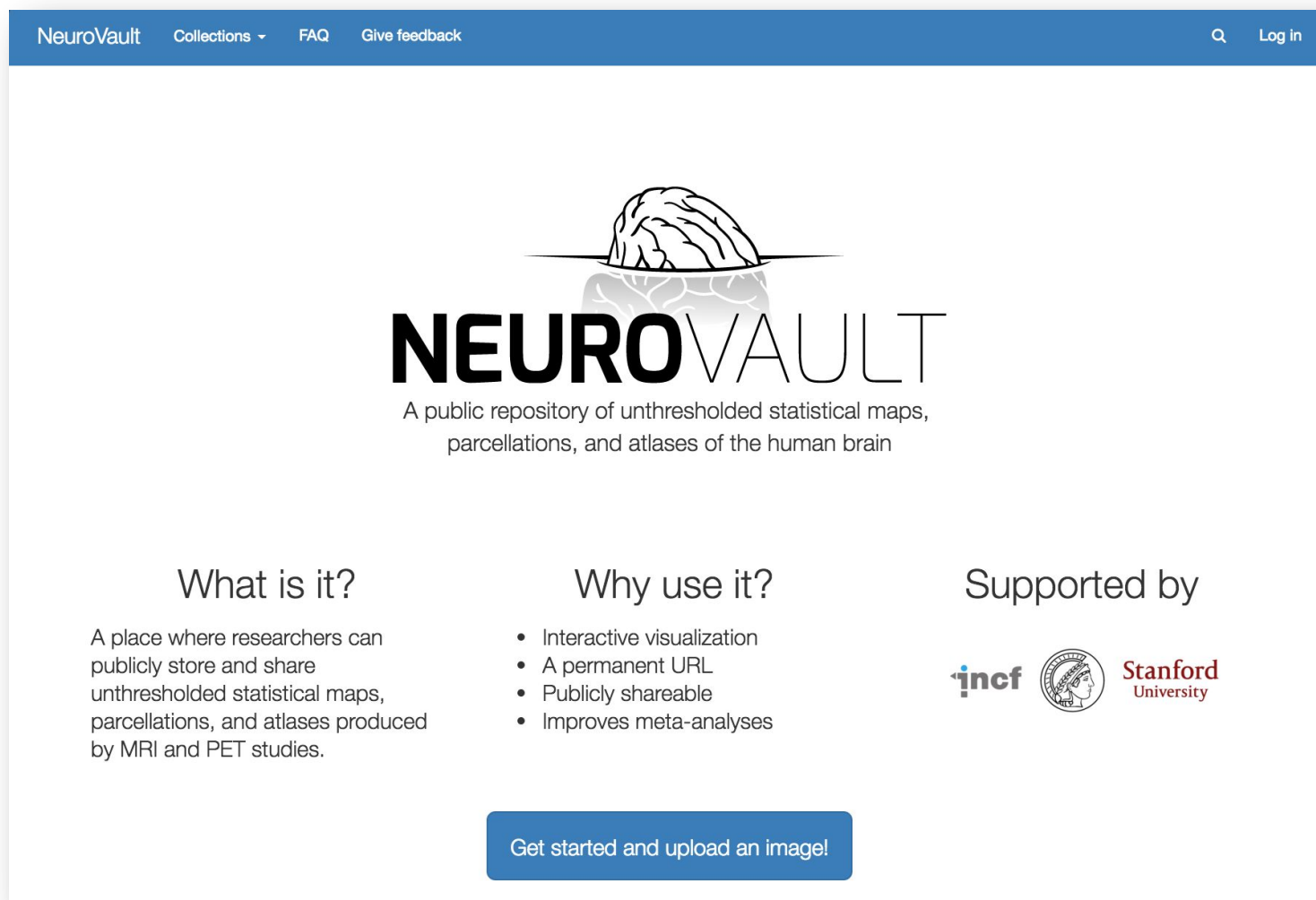
# Self Promotion Alert: Robustness of the meta-analytic estimators

Poster 2653




How to publish your statistic maps?

# Share your statistic maps



The screenshot shows the NeuroVault website homepage. At the top, there is a blue navigation bar with the text "NeuroVault" on the left, "Collections" with a dropdown arrow, "FAQ", and "Give feedback" in the center, and a search icon and "Log in" on the right. The main content area features a central logo consisting of a stylized brain with a horizontal line through it, and the text "NEUROVAULT" below it. Underneath the logo is the tagline: "A public repository of unthresholded statistical maps, parcellations, and atlases of the human brain". Below this, there are three columns of text. The first column is titled "What is it?" and describes the site as a place for researchers to store and share unthresholded statistical maps, parcellations, and atlases produced by MRI and PET studies. The second column is titled "Why use it?" and lists four bullet points: "Interactive visualization", "A permanent URL", "Publicly shareable", and "Improves meta-analyses". The third column is titled "Supported by" and features logos for "incf" (International Neuroinformatics Coordinating Framework), the University of California, and "Stanford University". At the bottom center, there is a blue button with the text "Get started and upload an image!".

NeuroVault Collections ▾ FAQ Give feedback Q Log in



## NEUROVAULT

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




### What is it?

A place where researchers can publicly store and share unthresholded statistical maps, parcellations, and atlases produced by MRI and PET studies.

### Why use it?

- Interactive visualization
- A permanent URL
- Publicly shareable
- Improves meta-analyses

### Supported by



Get started and upload an image!

<http://neurovault.org>

# Share your statistic maps

NeuroVault Collections ▾ FAQ Give feedback Q Log in

## A Correspondence between Individual Differences in the Brain's Intrinsic Functional Architecture and the Content and Form of Self-Generated Thoughts

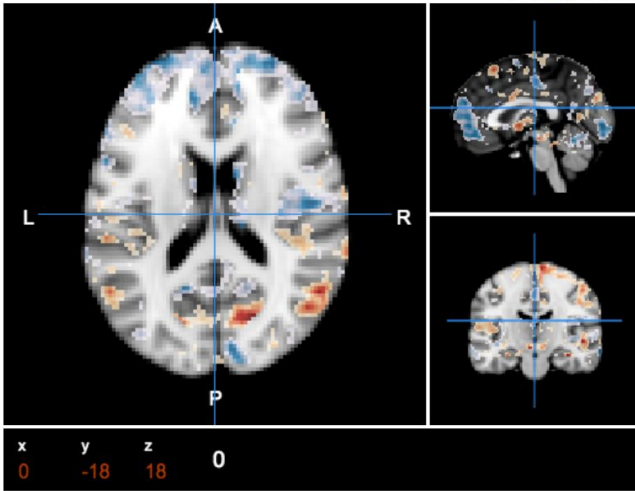
Contributed by ChrisFiloGorgolewski

Krzysztof J. Gorgolewski, Dan Lurie, Sebastian Urchs, Judy A. Kipping, R. Cameron Craddock, Michael P. Milham, Daniel S. Margulies, Jonathan Smallwood

[Link to the paper](#)

[3D View](#)

File View Options ■ ■ ■



x y z 0  
0 -18 18

[Images](#) [Details](#)

Show  entries Search:

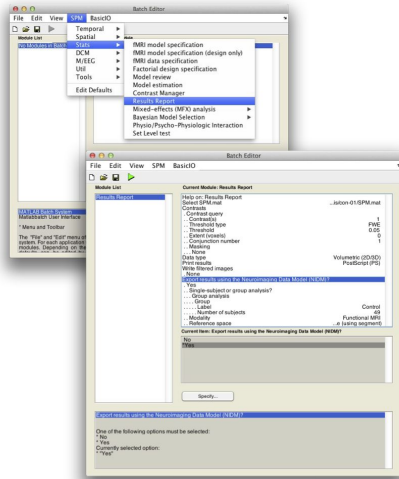
View	ID	Name	Type
<input type="checkbox"/>	25	fALFF: Past	Z map
<input type="checkbox"/>	26	fALFF: Future	Z map
<input type="checkbox"/>	27	fALFF: Past > Future	Z map
<input type="checkbox"/>	28	fALFF: Positive	Z map
<input type="checkbox"/>	29	fALFF: Negative	T map
<input type="checkbox"/>	30	fALFF: Positive > Negative	Z map
<input type="checkbox"/>	31	fALFF: Social Cognition	Z map

Showing 1 to 7 of 30 entries [First](#) [Previous](#) [Next](#) [Last](#)

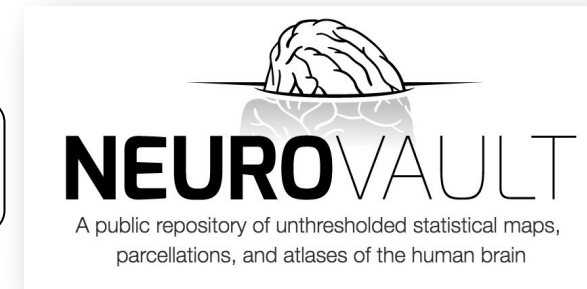
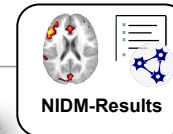
<http://neurovault.org>

# From SPM & FSL

SPM



Name	Size	Kind
beta_0001.nii	2.4 MB	NIFTI
con_0001.nii	2.4 MB	NIFTI
mask.nii	593 KB	NIFTI
nidm_001_nidm.zip	4.1 MB	ZIP archive
ResMS.nii	4.7 MB	NIFTI
RPV.nii	4.7 MB	NIFTI
SPM.mat	484 KB	MATLAB Data
spmT_0001.nii	2.4 MB	NIFTI

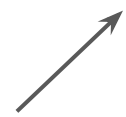


FSL

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



Name	Size	Kind
design.con	126 bytes	Document
design.fsf	20 KB	Document
design.grp	131 bytes	Document
design.icon	28 bytes	Document
cope1 feat	--	Folder
cope2 feat	--	Folder
inputreg	--	Folder
logs	--	Folder
lq_image.nii.gz	3.4 MB	gzip compressed archive
mask.nii.gz	15 KB	gzip compressed archive
mean_func.nii.gz	2.8 MB	gzip compressed archive
report_firstlevel.html	10 KB	HTML document
report_log.html	55 KB	HTML document
report_reg.html	17 KB	HTML document
report_stats.html	495 bytes	HTML document
report.html	922 bytes	HTML document
design.mat	732 bytes	MATLAB Data
design_cov.ppm	6 KB	OpenOffice.app Document
design.ppm	219 KB	OpenOffice.app Document
design_cov.png	106 bytes	Portable Network Graphics image
design.png	1 KB	Portable Network Graphics image
fsl_ds107_group.nidm.zip	13.6 MB	ZIP archive



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



# Conclusions

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

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# Conclusions

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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

