Meta-analysis and reproducibility

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FIU | FLORIDA INTERNATIONAL UNIVERSITY

Neurohackademy - Thursday, August 1, 2019 - Seattle, WA, USA

***Historical perspective*:** Before the *reproducibility crisis*™, we were interested in consensus across studies

<u>**Community Standards:**</u>

Spatial normalization to standard templates
Results reported as 3D coordinates (peaks)

This work collectively led to formal, quantitative meta-analyses, launched in the early to mid 2000's

***Historical perspective*: Before the *reproducibility crisis*™, we were interested in consensus across studies**

Limitations of neuroimaging studies

Small Samples
Compared to other fields of cognitive and social science, particularly to clinical research

Indirect Measure of Neuronal Activity
Reliability is limited by biological, technical, and methodological confounds

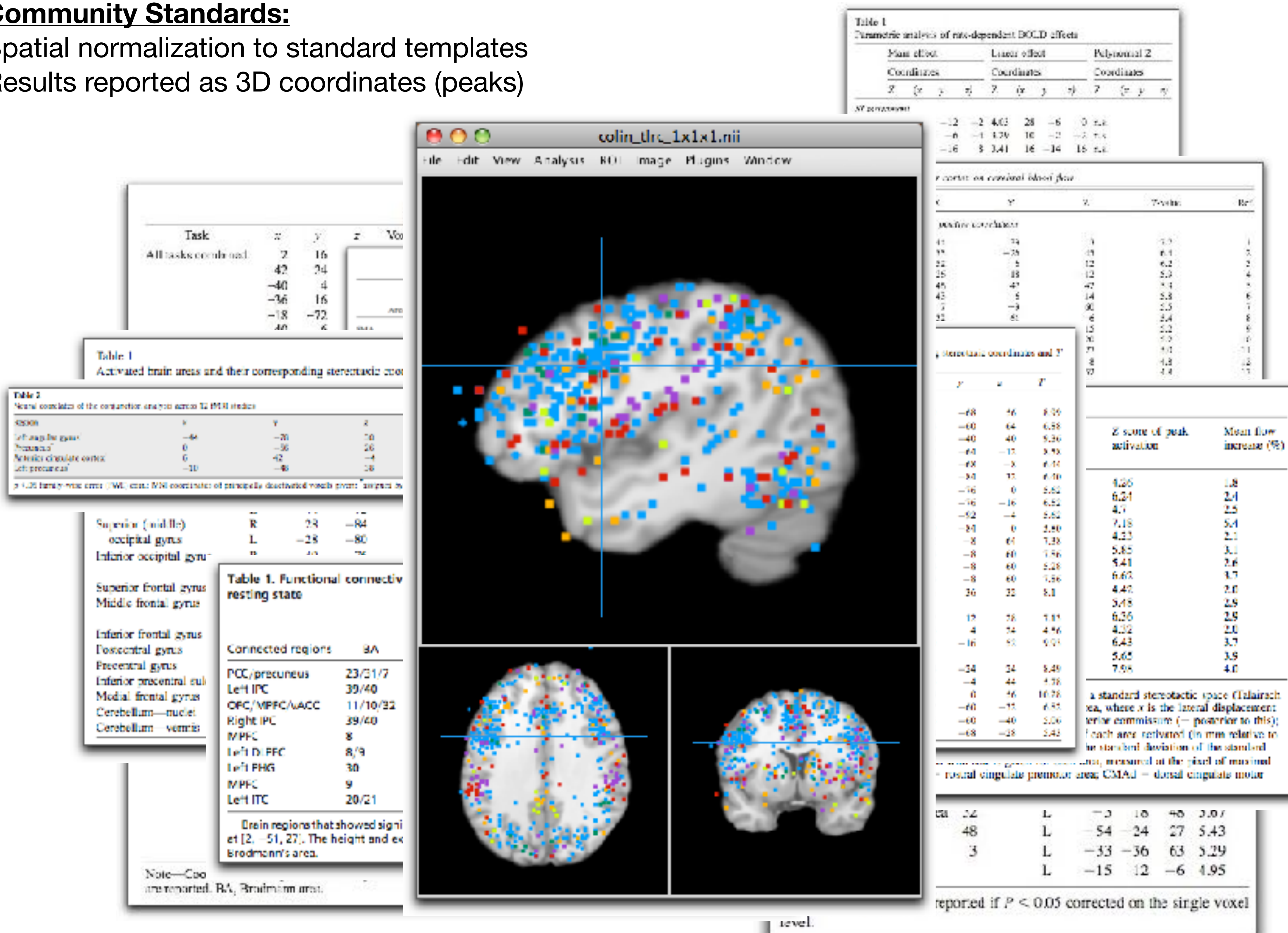
Publication of Isolated Findings
Due to logistics and expense, additional experiments for confirmation and extension are rare

Generalization of Context-Specific Findings
Inference on brain function and pathomechanisms is based on a specific observed difference between two conditions

Coordinate-Based Meta-Analysis

Where do the foci converge?

<u>Community Standards:</u>
Spatial normalization to standard templates
Results reported as 3D coordinates (peaks)

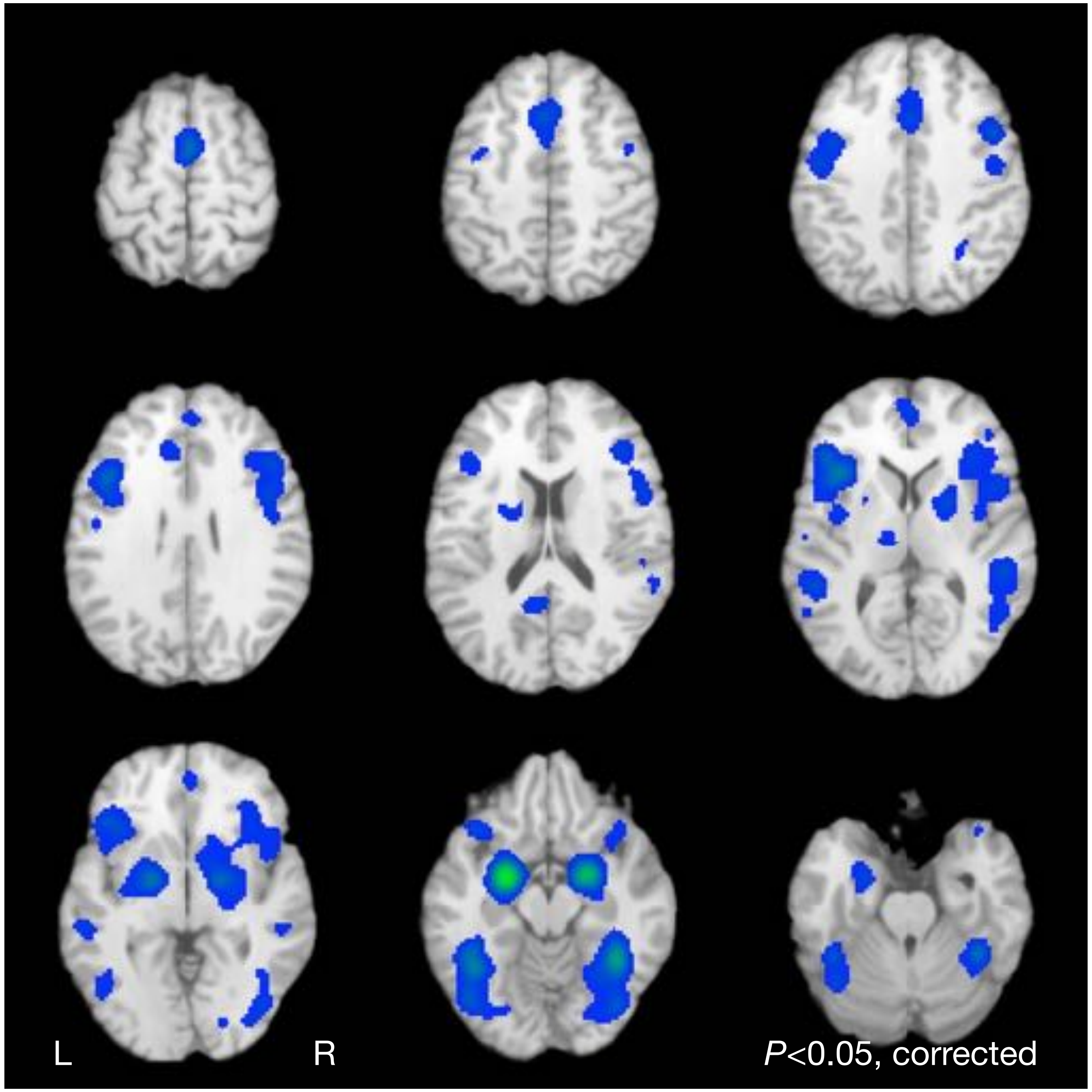


Coordinate-Based Meta-Analysis

Where do the foci converge?

- **Convolve foci with spatial kernel to produce study-specific modeled activation maps**
- **Combine those MA maps into a sample-wise map**
- **Compare to null distribution to determine voxel-wise statistical significance**

Activation Likelihood Estimation (ALE)



Coordinate-Based Meta-Analysis

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Activation Likelihood Estimation (ALE)
Kernel Density Analysis (KDA)
Multilevel Kernel Density Analysis (MKDA)
Specific Coactivation Likelihood Estimation (SCALE)
Seed-Based d-Mapping
MKDA Chi2 Extension

Described in detail by
Samartsidis et al., Stat Sci, 2017

Image-Based Meta-Analysis

Where do the images converge?

Mixed-Effects GLM (gold standard)
Fixed-Effects GLM
Fisher's IBMA
Stouffer's IBMA
z permutation

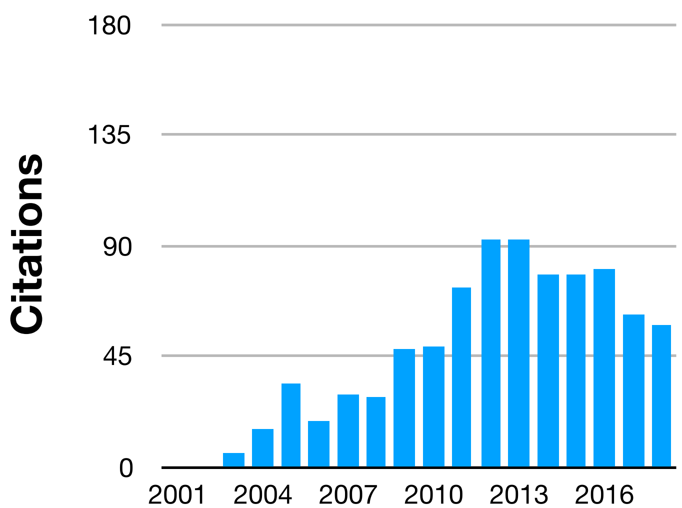
Described in detail by Maumet and Nichols, 2016
doi: https://doi.org/10.1101/048249

Please upload your maps!

NEUROVAULT

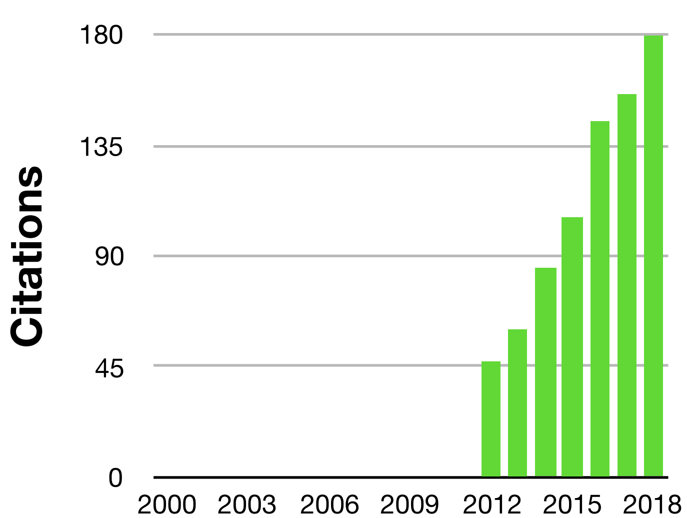
The Rising Popularity of Meta-Analyses

Introduction of ALE Approach



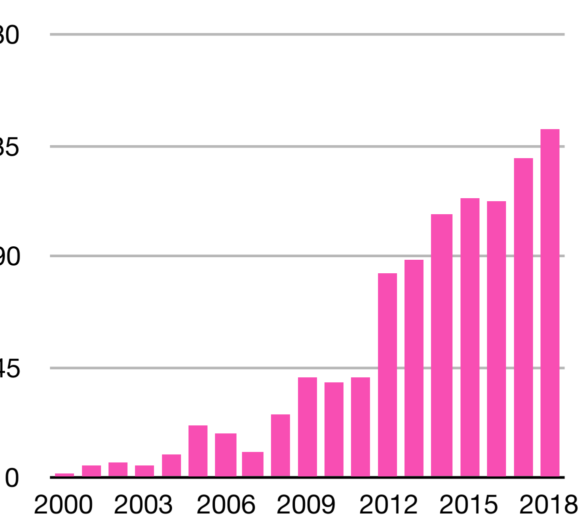
Turkeltaub et al., Neuroimage, 2002

Introduction of Neurosynth



Yarkoni et al., Nat Methods, 2011

fMRI + Meta-Analysis



What Can Meta-Analysis Do For You?

Identifying consensus (or the lack thereof) is always a good thing

I am starting a new project :

1. Great introduction to a new topic

I am mentoring an undergrad and don't know what to assign them:

2. Feasible project for your novice trainees

I am an experienced researcher:

3. Systematic analysis of variability (e.g., participants, tasks) can resolve conflict in a given community

4. Validate a new task or data acquisition approach

5. ROI selection

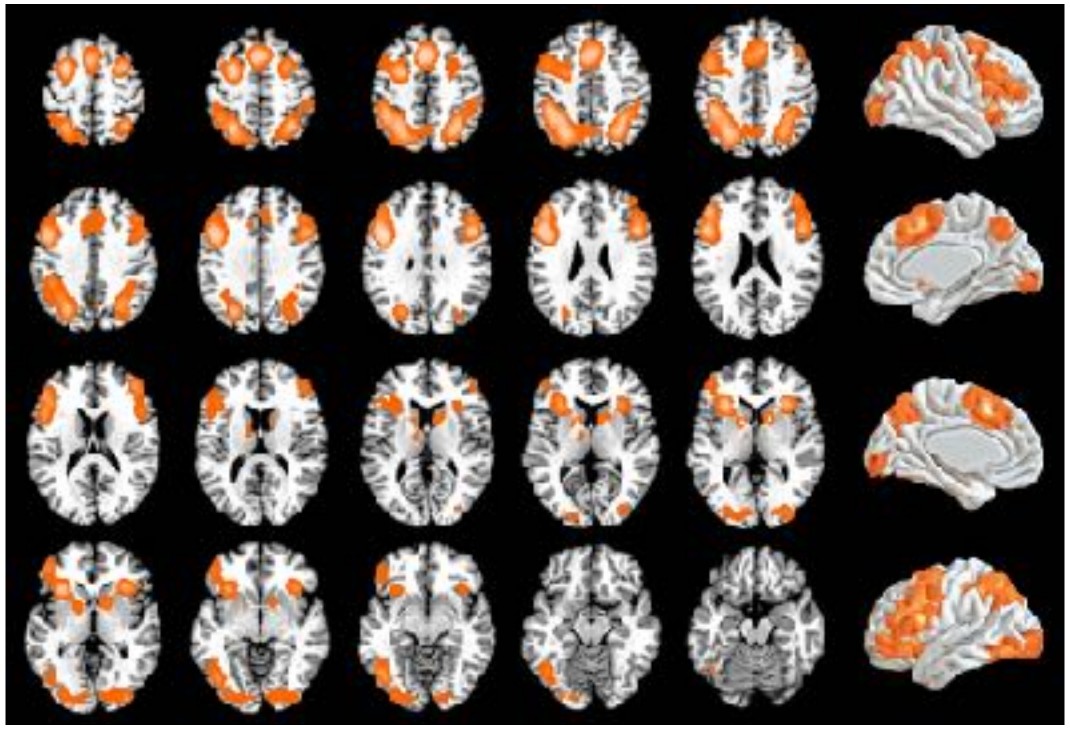
6. Functional decoding

7. Data-driven approach to validate cognitive models

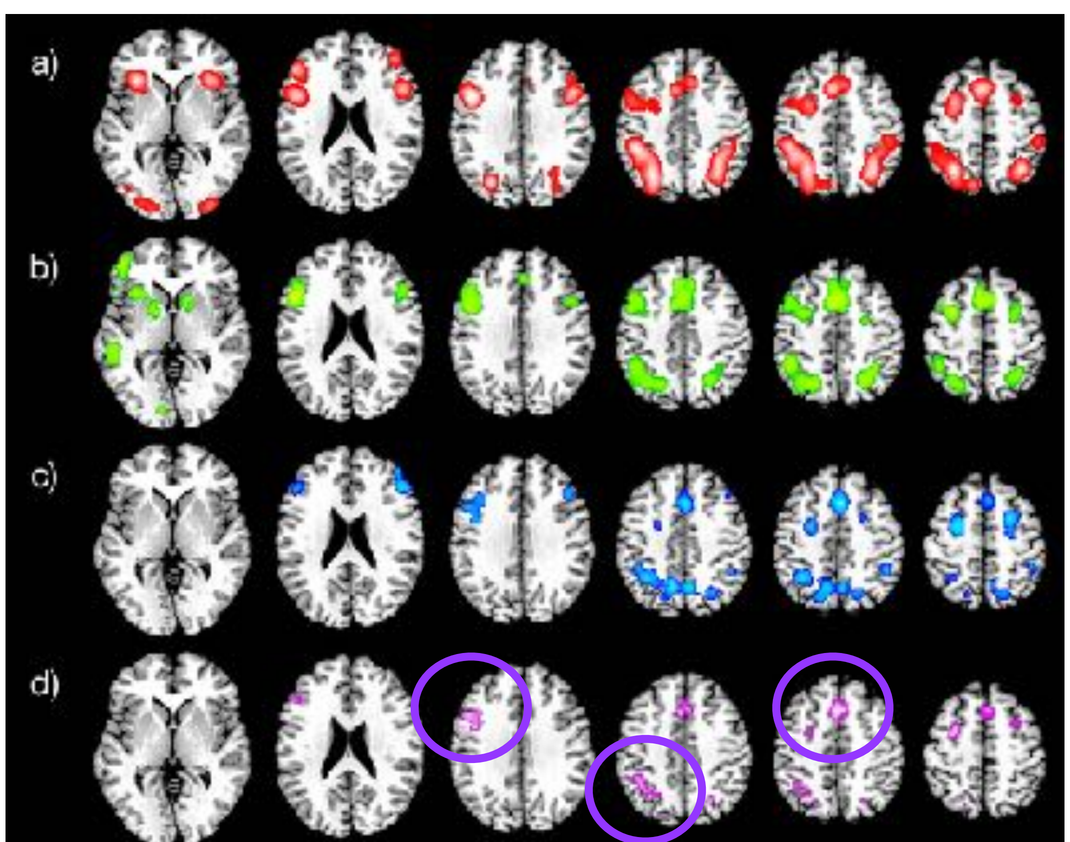
Example

ROI Selection

Meta-Analysis of Problem Solving

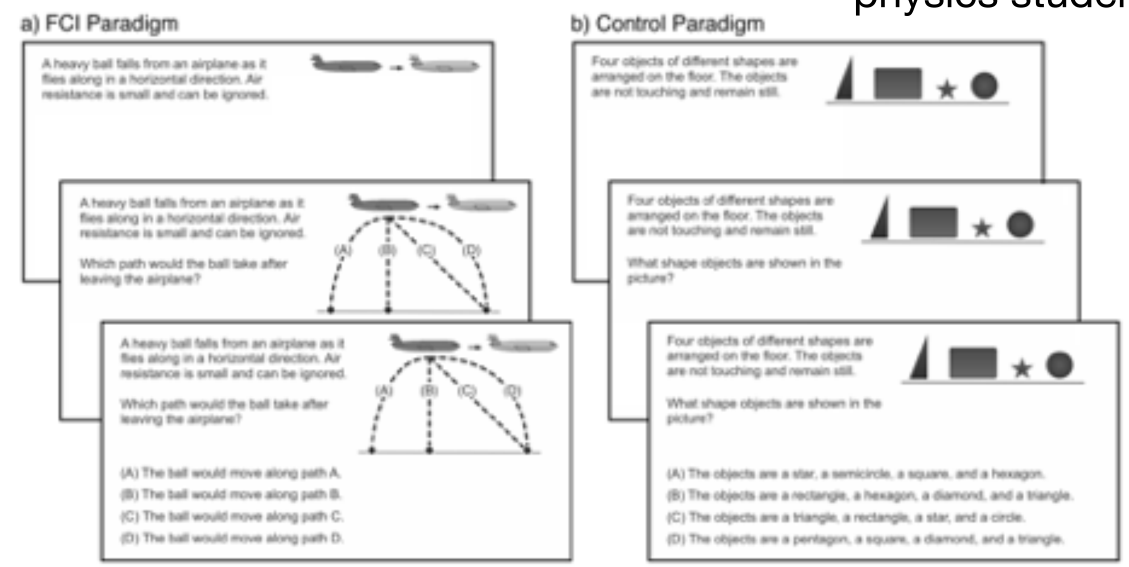


Bartley et al., Neurosci Biobehv Rev, 2018

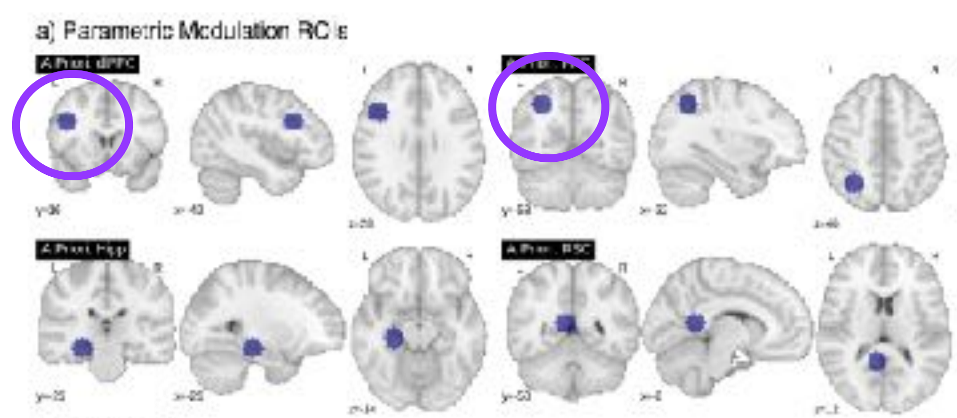


Force Concept Inventory (FCI)

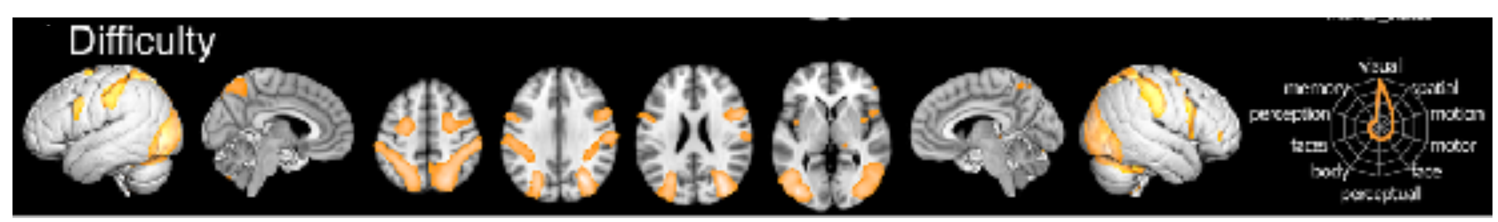
107 undergraduate physics students



H: accuracy, difficulty, strategy associated with problem solving and memory



Memory ROIs:
Robinson et al., HBM, 2015
Andrew-Hanna et al., NI, 2014
(declarative and autobiographical)



- We found that difficulty, but not accuracy or strategy, modulate brain activity during physics problem solving.
- Problem solving network engaged regardless of whether a correct answer was achieved and does not reflect students' perception of their reasoning strategy.
- Mental states associated with visualization, spatial/motion perception and memory engaged when difficulty

PREPRINT: http://dx.doi.org/10.1101/526574

Bartley et al., In Revision

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Example

Functional Decoding

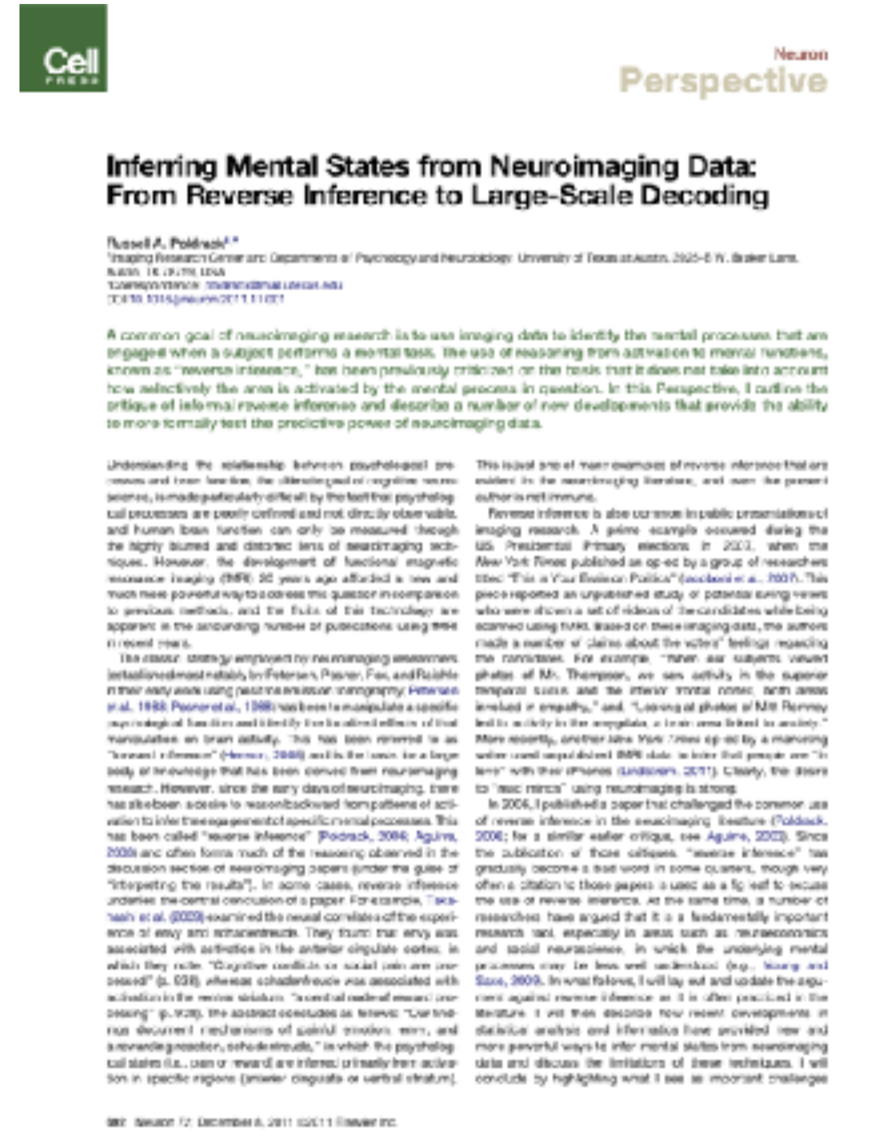

Can cognitive processes be inferred from neuroimaging data?

Russell A. Poldrack

Department of Psychology and Brain Research Institute, UCLA, Los Angeles, CA 90095-1563, USA

Introduction

Inference in neuroimaging


Neuron

Perspective

Inferring Mental States from Neuroimaging Data: From Reverse Inference to Large-Scale Decoding

Russell A. Poldrack

Discussion: interpret findings, *what does this region do?*

Forward Inference: given performance of task X, brain activity was observed in region Y

fear task activates the amygdala

Reverse Inference: given brain activity in region X, therefore mental function Y was engaged

the amygdala was activated, thus fear was engaged

*There are certainly papers that have shaped my worldview, and I think that's true for everyone. We are not machines after all - we can't read *all* the papers.*

Example

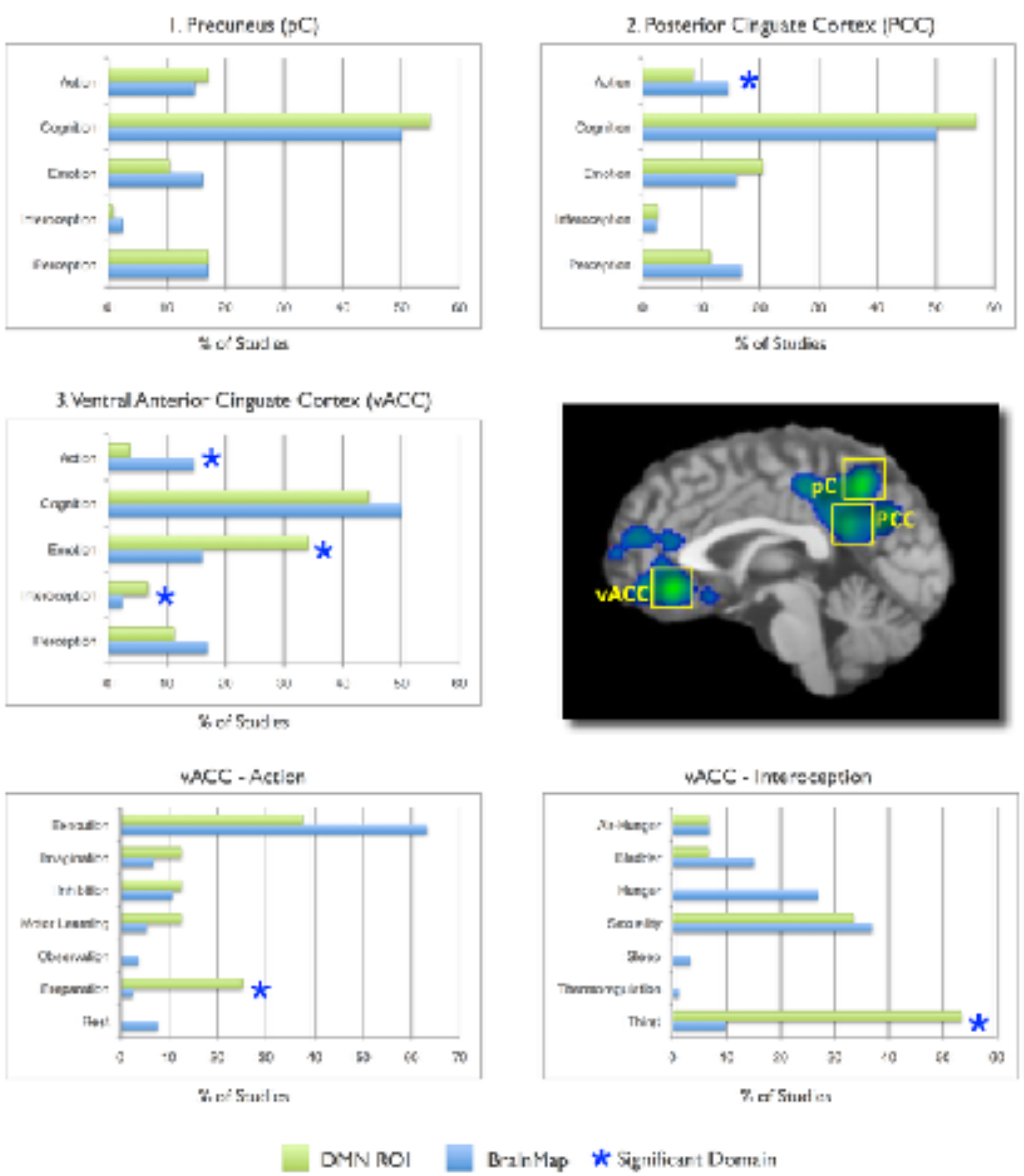
Functional Decoding

"recent developments in statistical analysis and informatics have provided new and more powerful ways to infer mental states from neuroimaging data" BrainMap and Neurosynth databases

"reverse inference can be a very useful strategy, especially if it is based on real data (such as the meta-analytic maps of from Yarkoni et al., 2011) rather than on an informal reading of the literature"

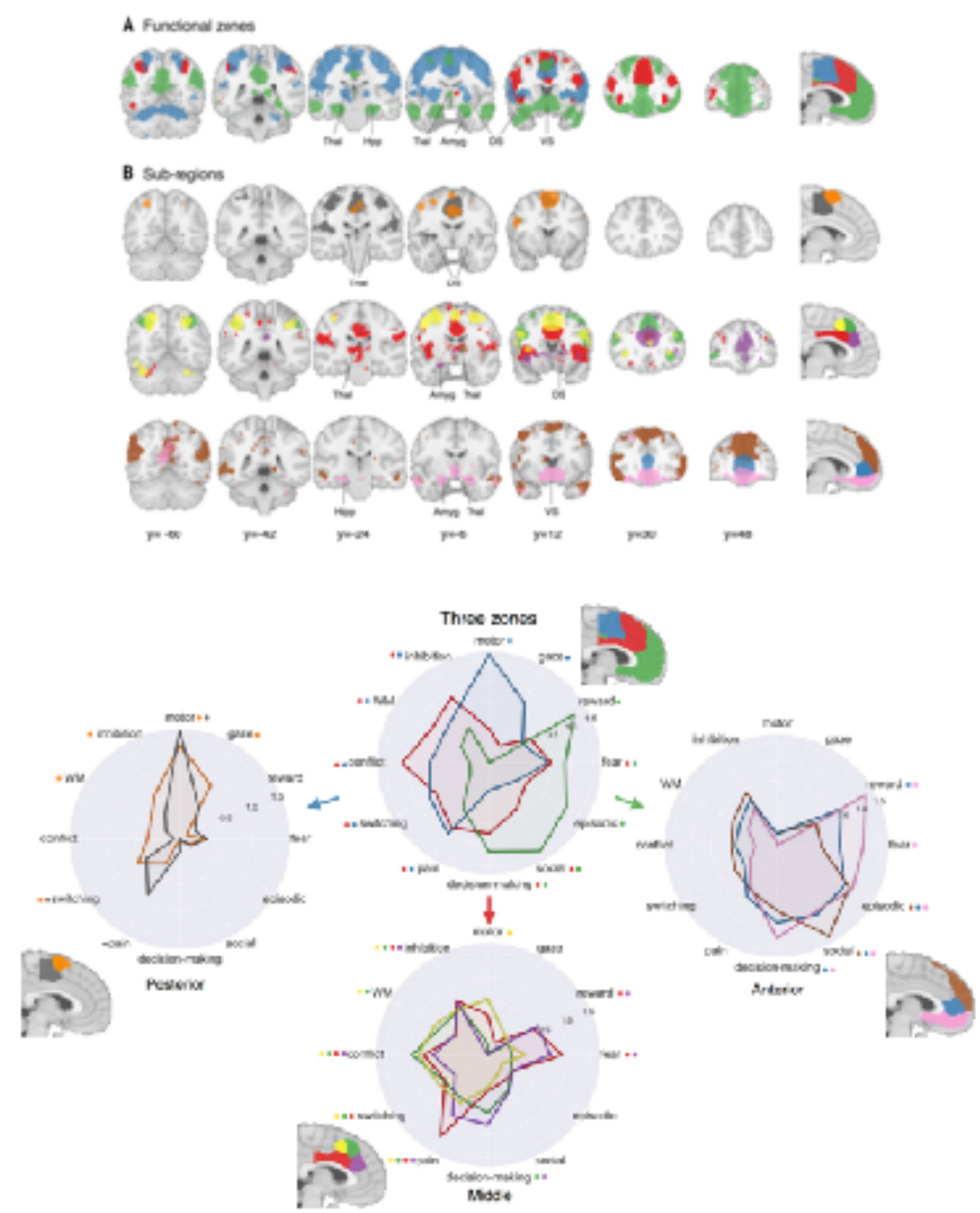
Poldrack, Neuron, 2011

Investigating the heterogeneity of the default mode network using coordinate-based meta-analytic modeling



Laird et al., J Neurosci, 2009

Large-scale meta-analysis of human medial frontal cortex reveals tripartite functional organization



de la Vega et al., J Neurosci, 2016

Example

Functional Decoding

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“reverse inference can be a very useful strategy, especially if it is based on real data (such as the meta-analytic maps of from Yarkoni et al., 2011) rather than on an informal reading of the literature”

Poldrack, Neuron, 2011

- Large-scale meta-analytic databases consolidate results from many studies and annotate them to make them searchable
- Integrated algorithms make performing meta-analyses easier
- BrainMap and Neurosynth have complementary strengths and weaknesses

	BrainMap	Neurosynth
Created in	1994	2011
Annotation method	Manual	Automated
Annotation unit	Experiment	Paper
Size	3,010	11,406

Both offer tools/ methods for meta-analysis and decoding

Slide courtesy of Taylor Salo

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4. **Validate a new task or data acquisition approach**

5. **ROI selection**

6. **Functional decoding**

7. **Data-driven approach to validate cognitive models**

Example

Data-Driven Validation of Cognitive Models

- More resources are being deployed for the management, sharing, and meta-analysis of neuroimaging big data; this includes knowledge representation systems (e.g., ontologies)
- However, cognitive data descriptors are relatively under-developed (even a listing of the sub-types of a paradigm or mental function is challenging due to lack of consensus)
- **Why not let the data facilitate consensus?**

Overall Premise: differences in activation patterns across studies should be captured and leveraged as they indicate meaningful segregations in brain function

Tasks activating similar brain networks should be grouped as functionally similar in a cognitive schema

Tasks demonstrating differential activation patterns should be classified as functionally distinct

Example

Data-Driven Validation of Cognitive Models

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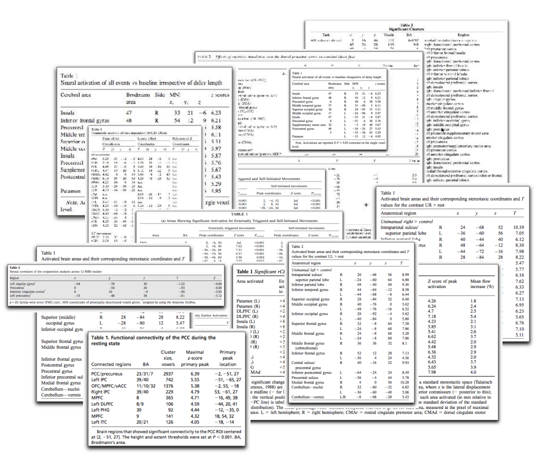
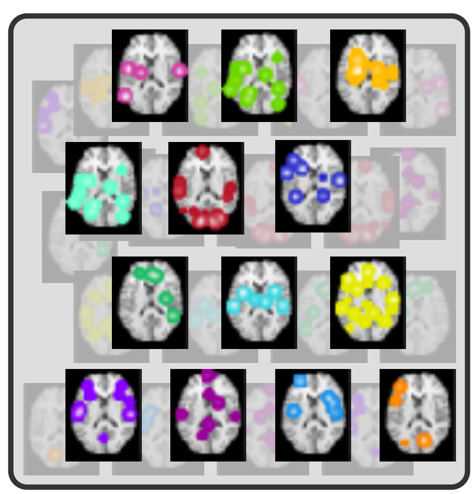
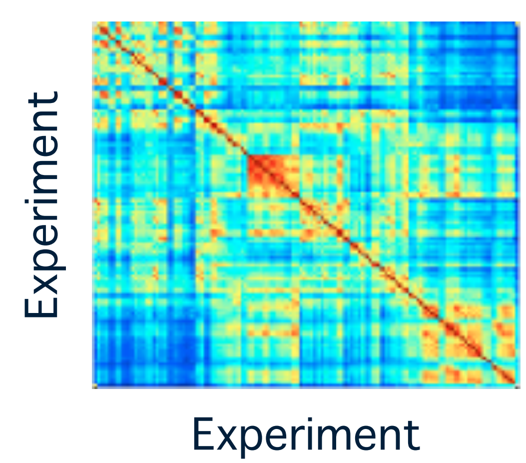
Extract Coordinates from Literature	Generate Modeled Activation Maps	Generate Correlation Matrix	Perform Clustering of Modeled Activation Maps

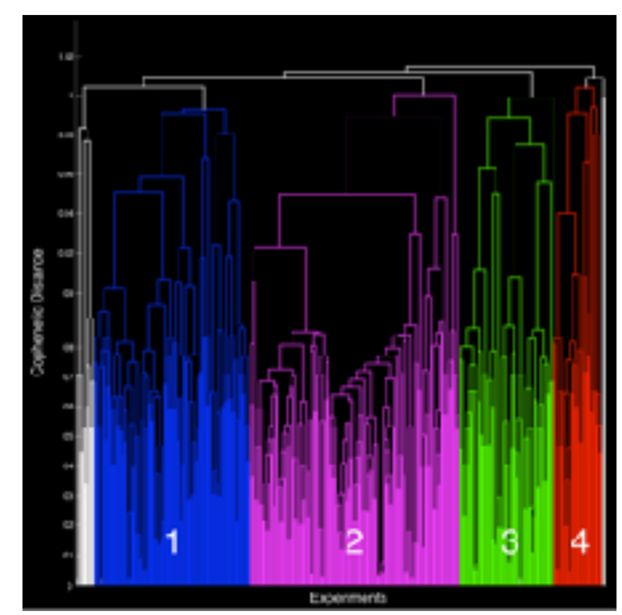




The whole brain sets of coordinates were blurred using a Gaussian distribution (FWHM defined by Eickhoff et al., 2009), filtered through a gray matter mask, and concatenated to form an experiment-by-voxel array



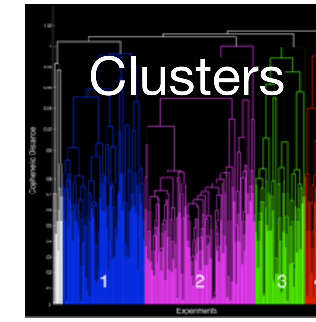
Correlation Matrix: correlation coefficients were computed to form an experiment-by-experiment matrix of activation patterns



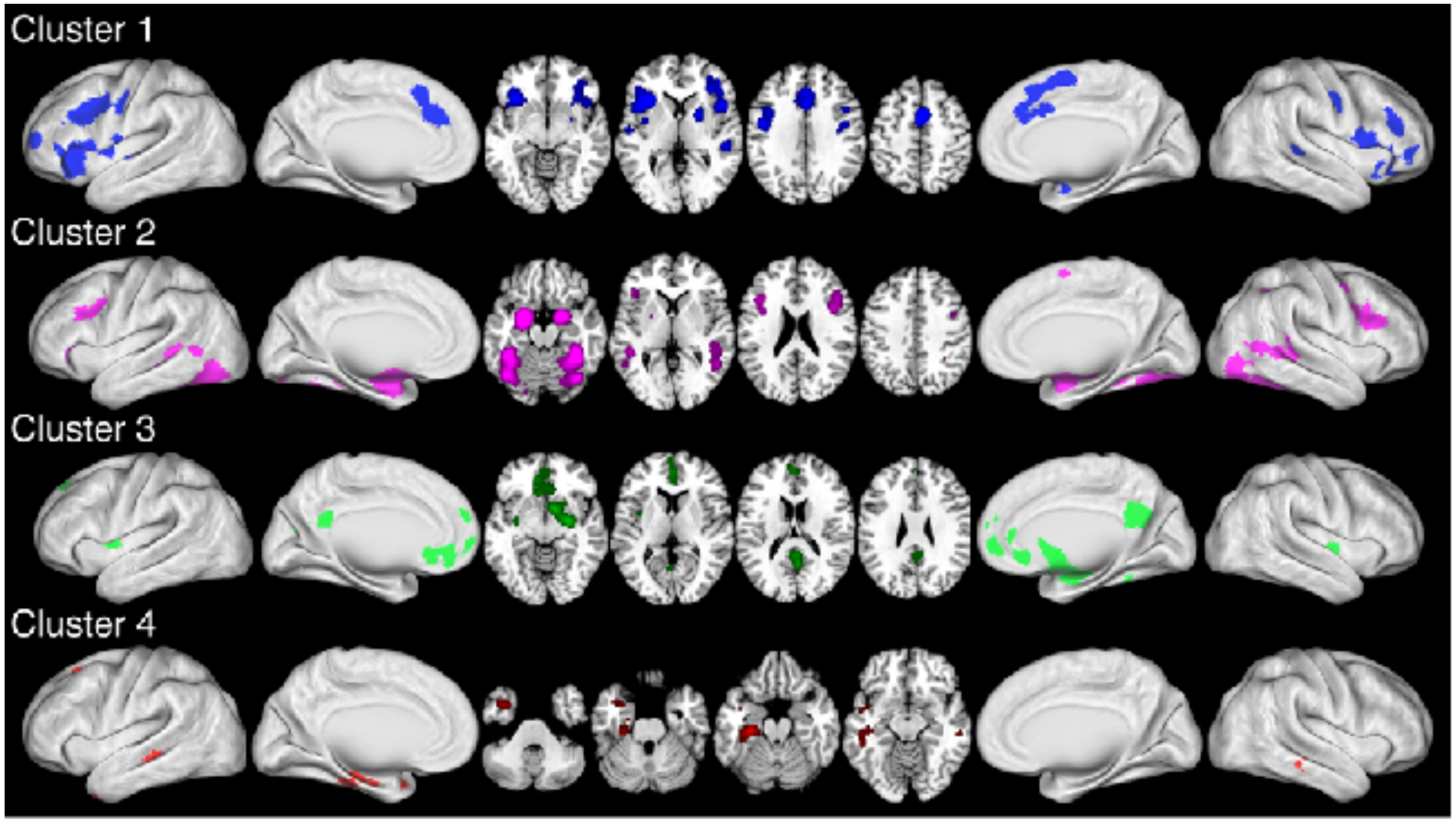
Hierarchical Clustering Analysis applied to the correlation matrix to identify clusters of experiments with similar activation patterns, generate ALE map, analyze metadata

Example

Data-Driven Validation of Cognitive Models



Face Perception Tasks



Visuospatial Attention and Visuomotor Coordination to Faces

Salience Network (bilateral insula and anterior cingulate)

Perception and Recognition of Faces

Amygdala, fusiform face area, occipito-temporal areas

Social Processing and Episodic Recall of Faces

Default Mode Network (MPFC and precuneus)

Face Naming and Lexical Retrieval

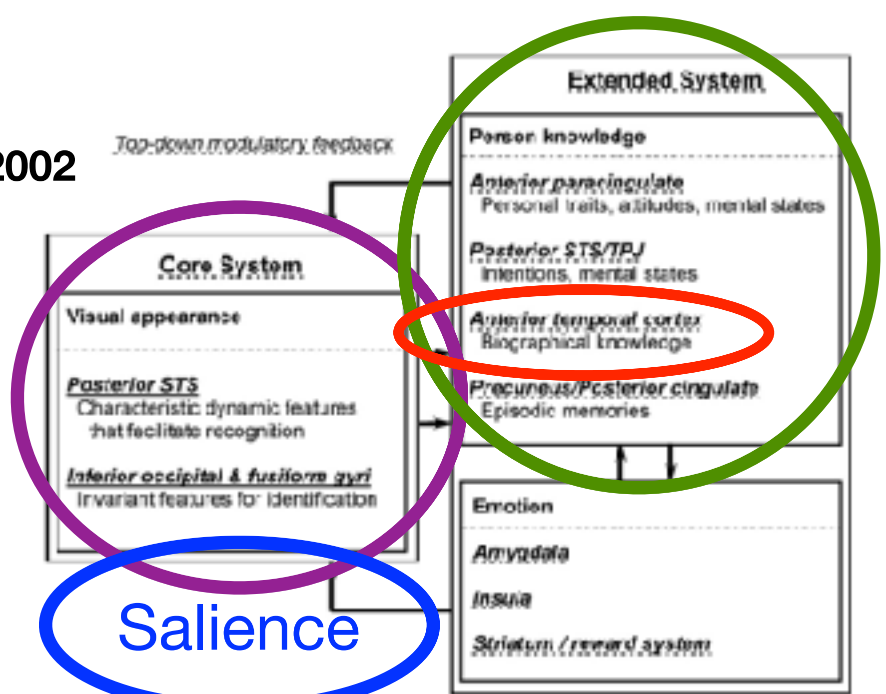
Middle temporal gyrus and inferotemporal cortex, temporal pole, parahippocampal gyrus

How well do our current results align?

Gobbini and Haxby, 2002

Laird et al., Neuroimage, 2015

- Confirm and extend a well-known cognitive model of face perception
- Our results demonstrate that a large-scale data mining approach can inform the evolution of cognitive models by meta-analytically probing the range of behavioral manipulations across experimental tasks



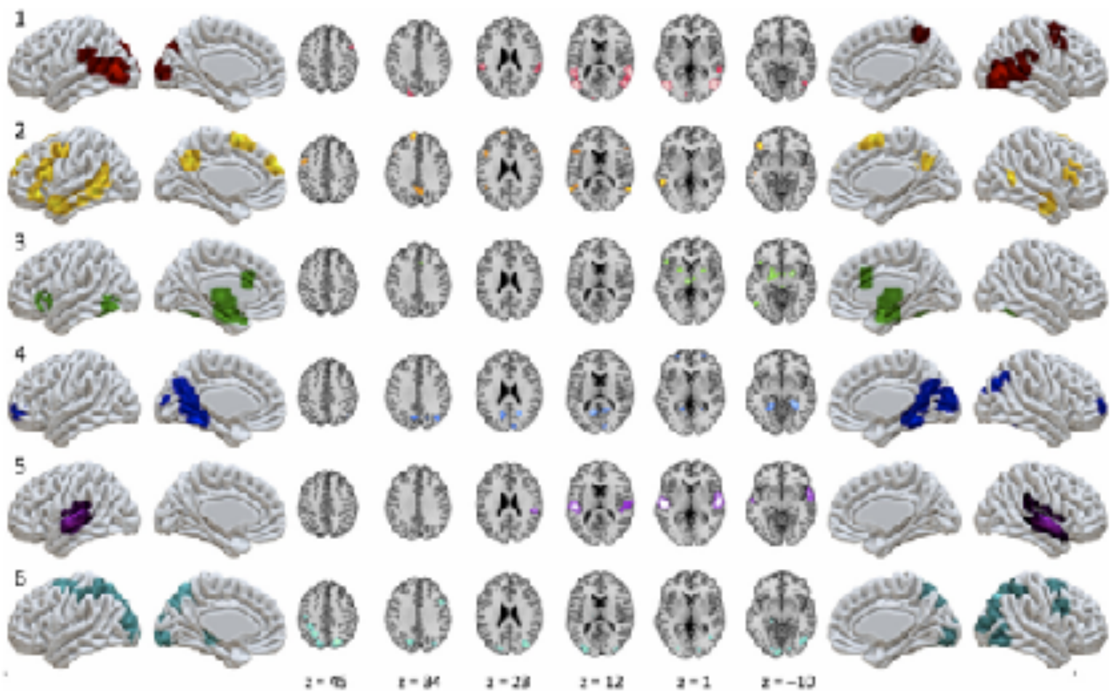
Example

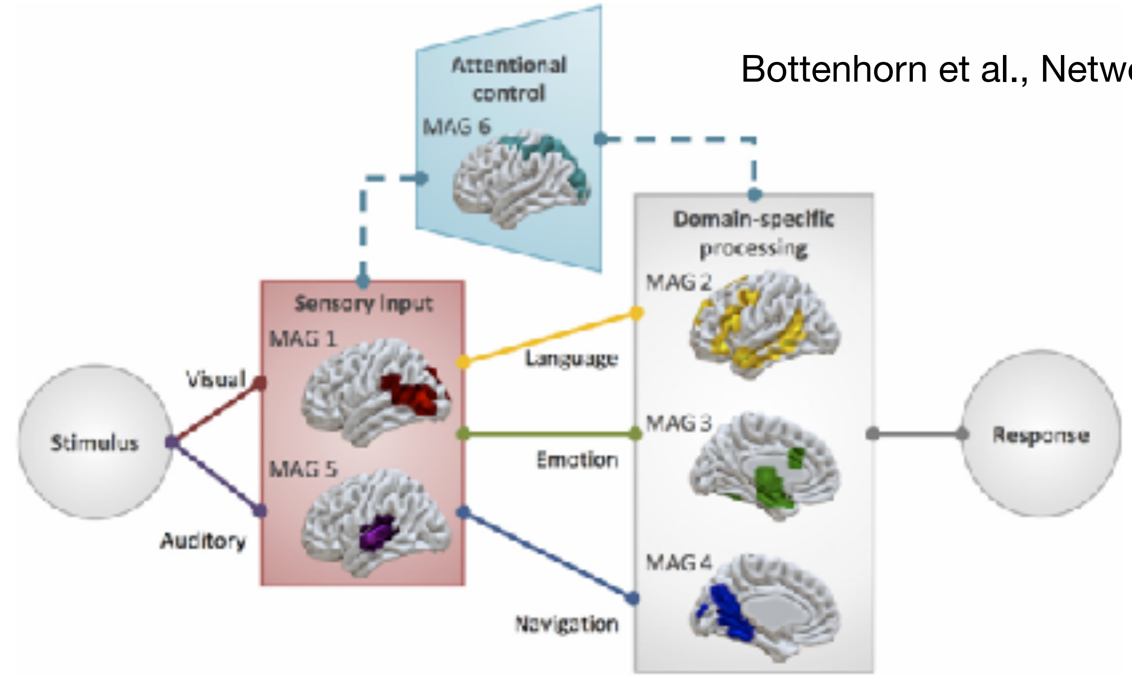
Data-Driven Validation of Cognitive Models

Naturalistic Tasks

Cooperating yet distinct brain networks engaged during naturalistic paradigms

Bottenhorn et al., Network Neurosci, 2018

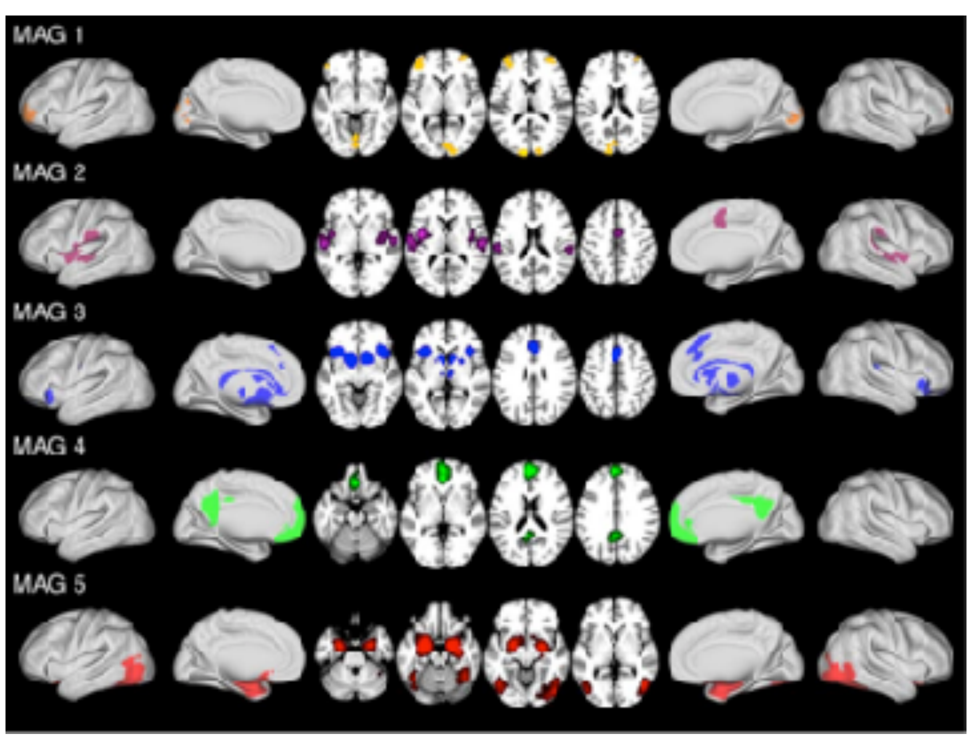


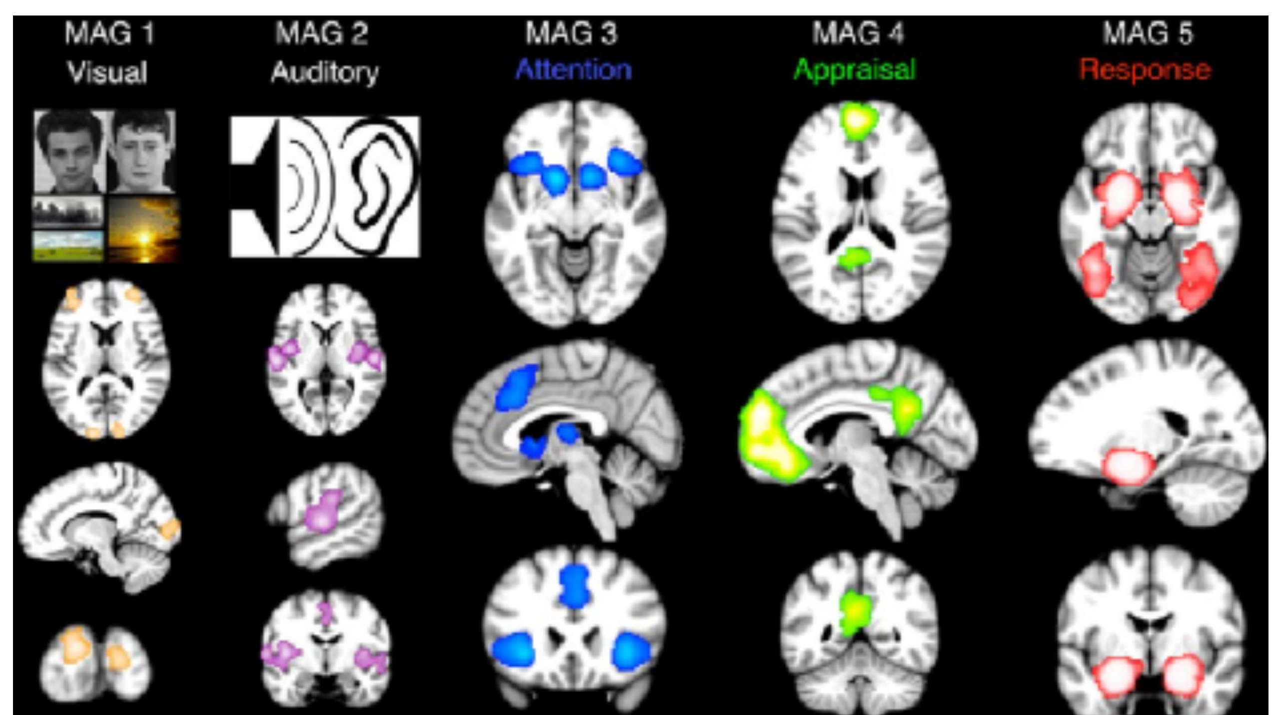


Emotional Tasks

Dissociable meta-analytic brain networks contribute to coordinated emotional processing

Riedel et al., HBM, 2018





MAG = meta-analytic grouping

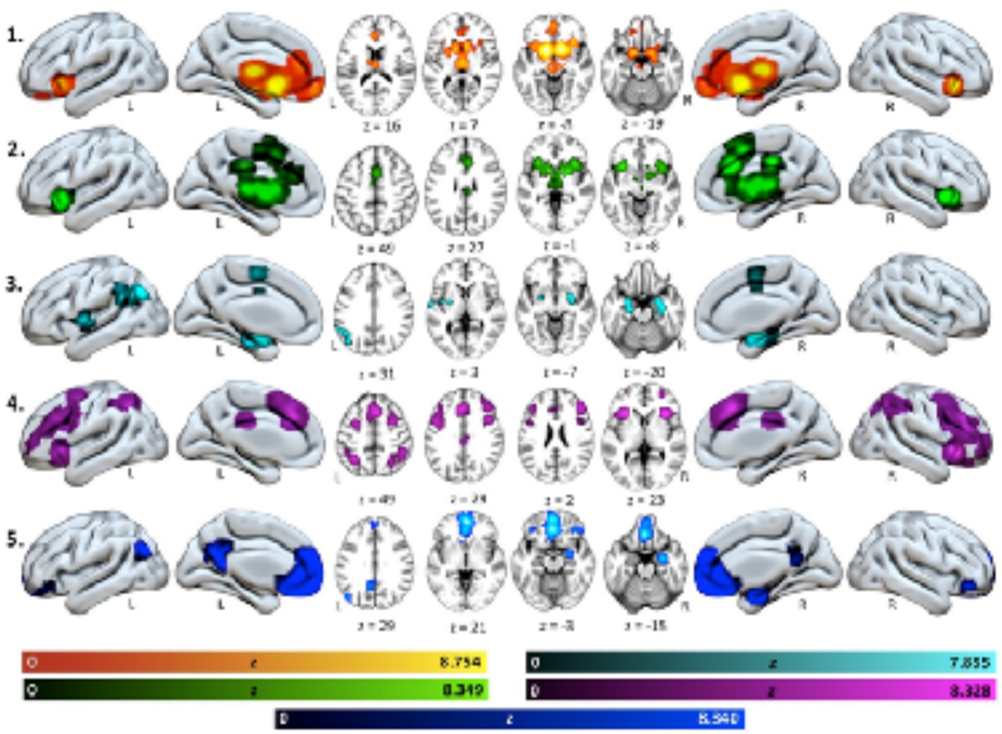
Example

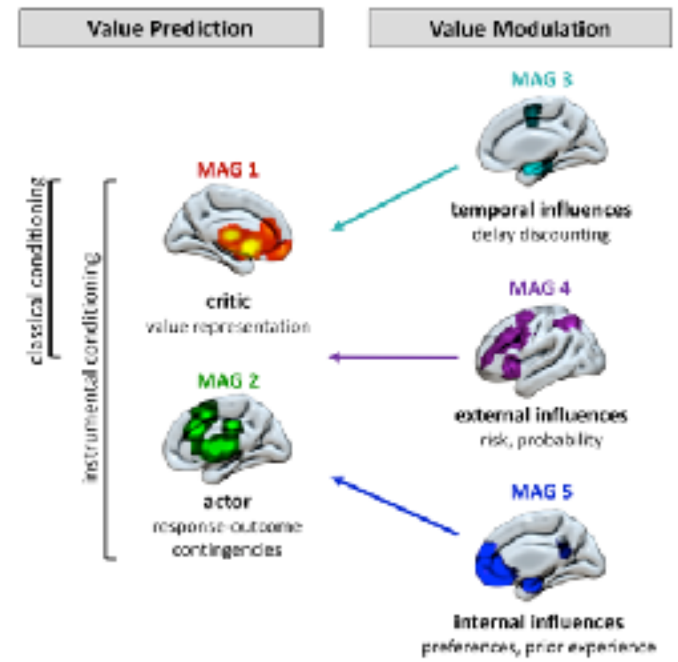
Data-Driven Validation of Cognitive Models

Reward Tasks

Meta-analytic clustering dissociates brain activity and behavior profiles across reward processing paradigms

Flannery et al., In Revision

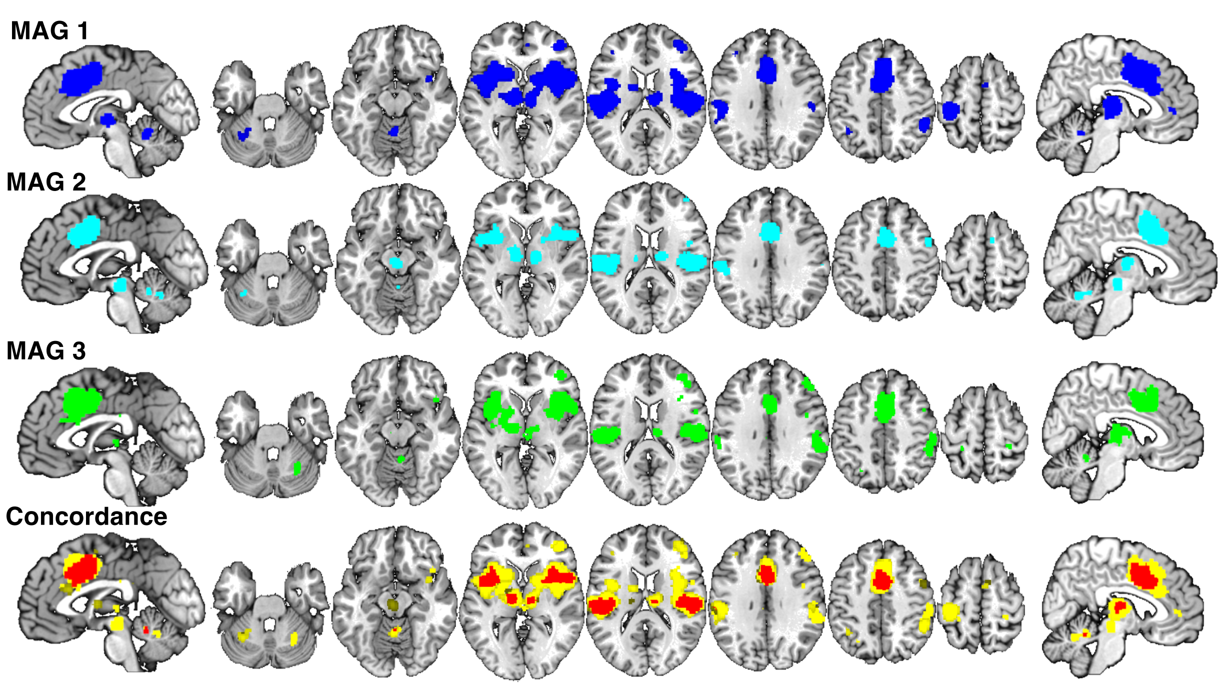


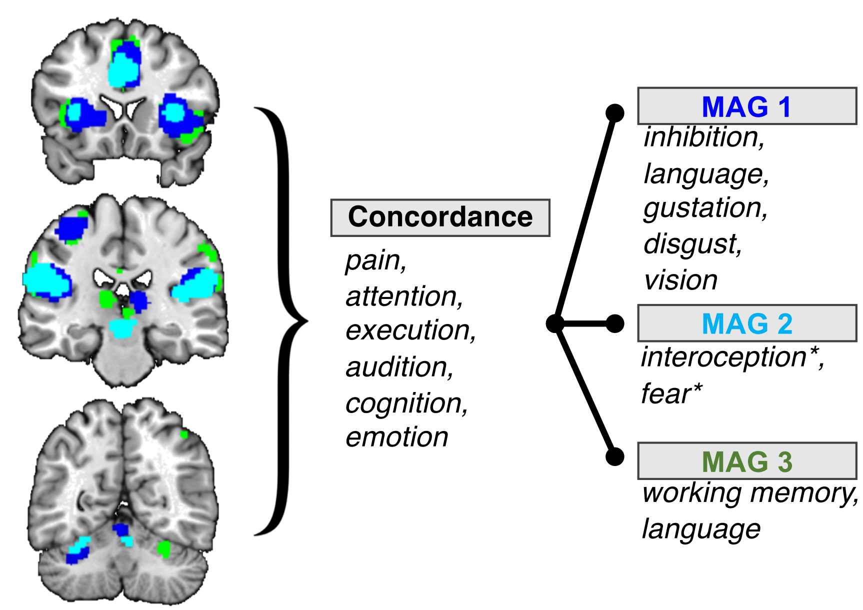


Pain Tasks

Data mining reveals discrete neurobiological systems that contribute to pain processing

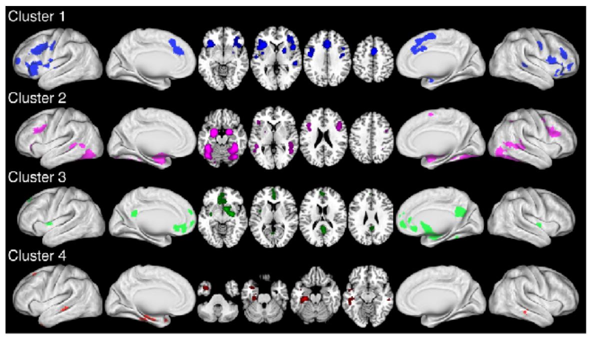
Yanes et al., In Preparation





***Personal perspective*: Starting at so many meta-analytic images for 15+ years reframes how you think about brain networks**

Face Perception Tasks



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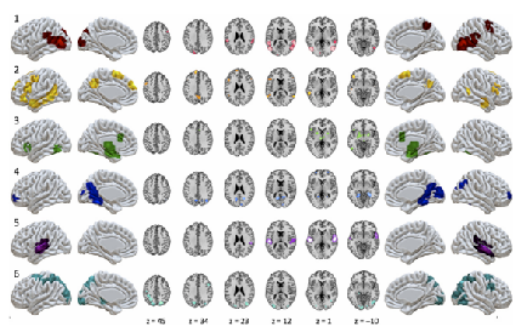
Naturalistic Tasks



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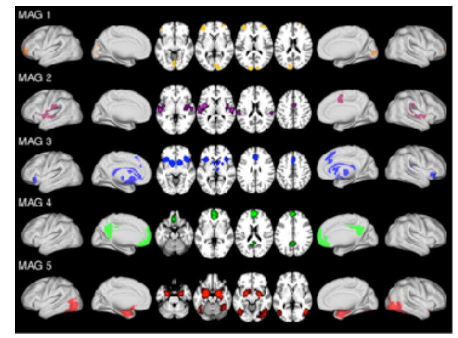
Emotional Tasks



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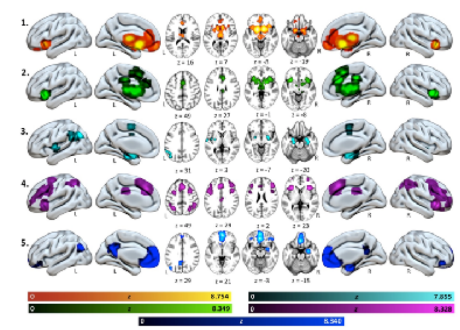
Reward Tasks



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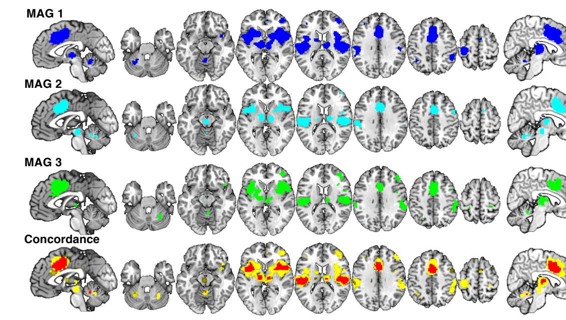
Pain Tasks



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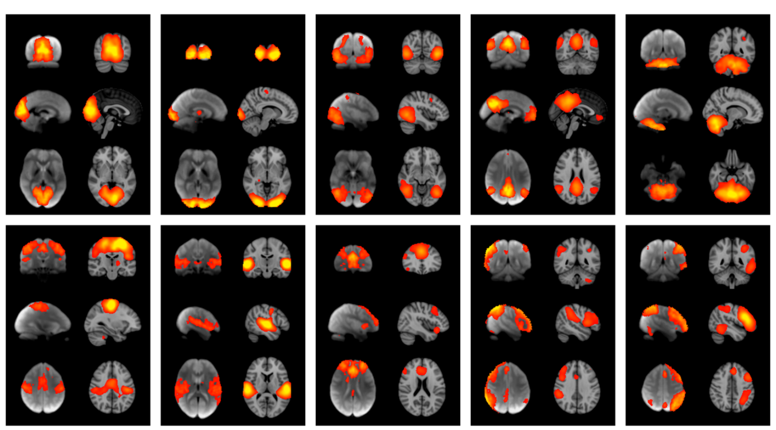
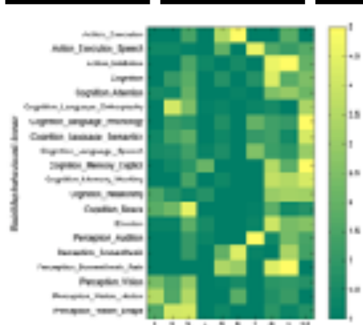
Salience Network **Default Mode Network** **Central Executive Network**

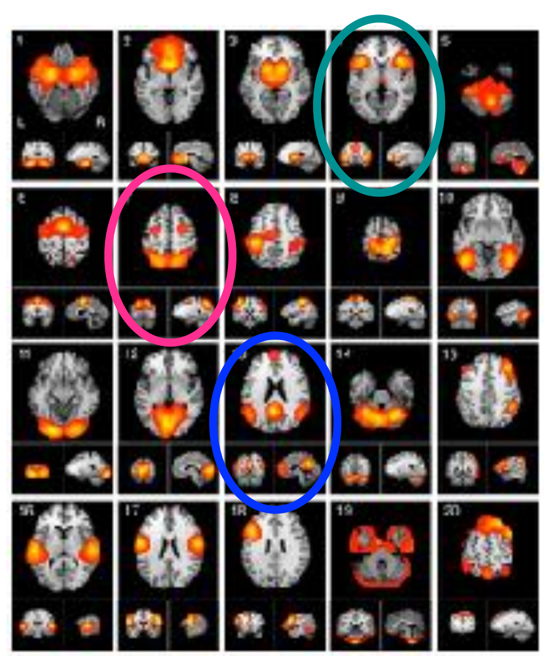
Large-Scale Meta-Analytic Data Mining





Correspondence of the brain's functional architecture during activation and rest

Smith et al., PNAS, 2009



Laird et al., J Cogn Neuro, 2011

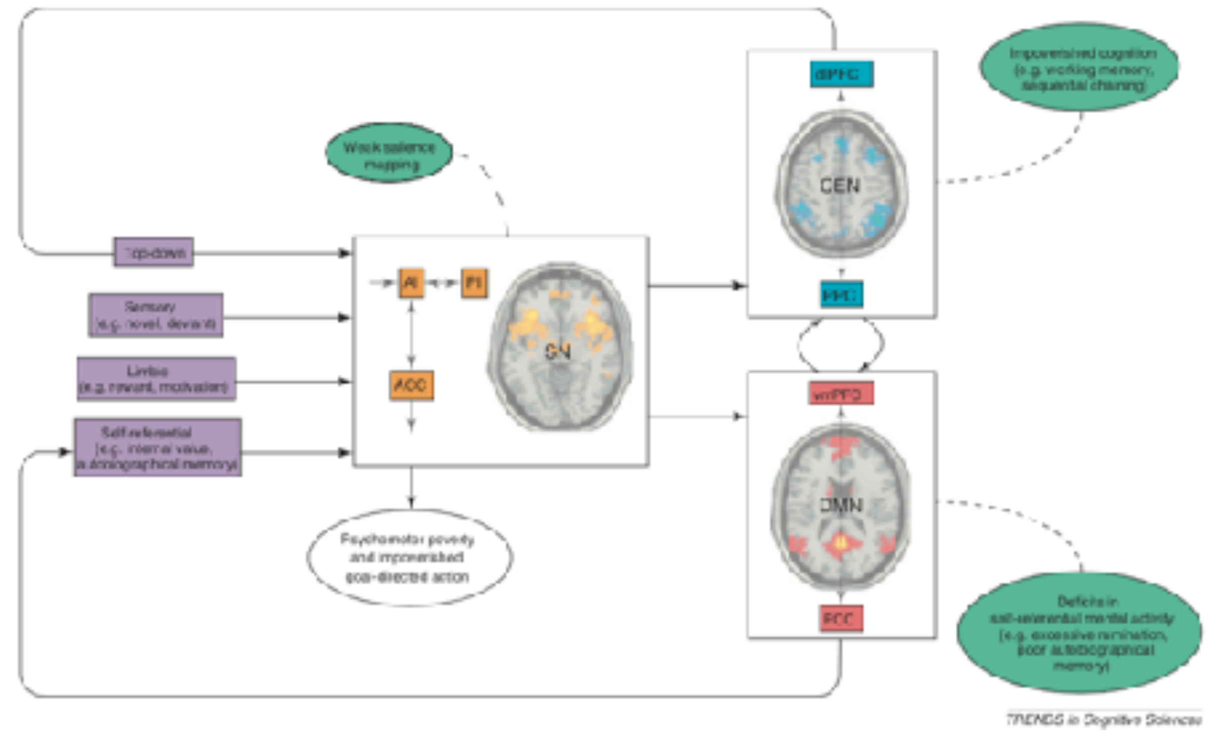

What is the most interesting part of the brain?

Behrens et al., TICS, 2013

Large-Scale Brain Networks

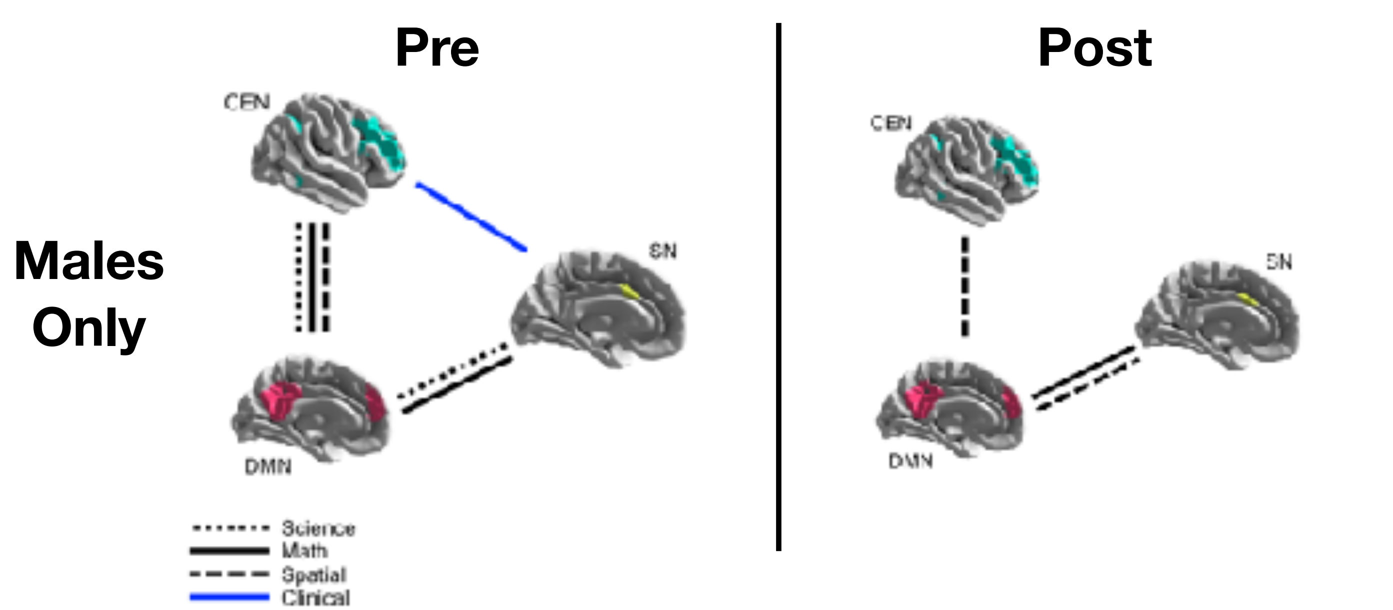
- Psychopathological processes, especially those found in mood disorders, are commonly associated with **aberrant connectivity within and between**:
    - the salience network (**SN**),
    - the default mode network (**DMN**),
    - and the central executive network (**CEN**)
- The interaction of these three, core networks underlies a unifying **triple network model** that characterizes the maladaptive network organization and function in psychiatric disorders
    - Dysfunctional connectivity in these networks can lead to diminished cognitive ability, and diminished control over self-referential processes such as rumination

Aberrant interconnectivity of the SN, CEN, and DMN is characteristic of **many psychiatric disorders**



Menon, TICS, 2011

Sex differences in brain correlates of STEM anxiety



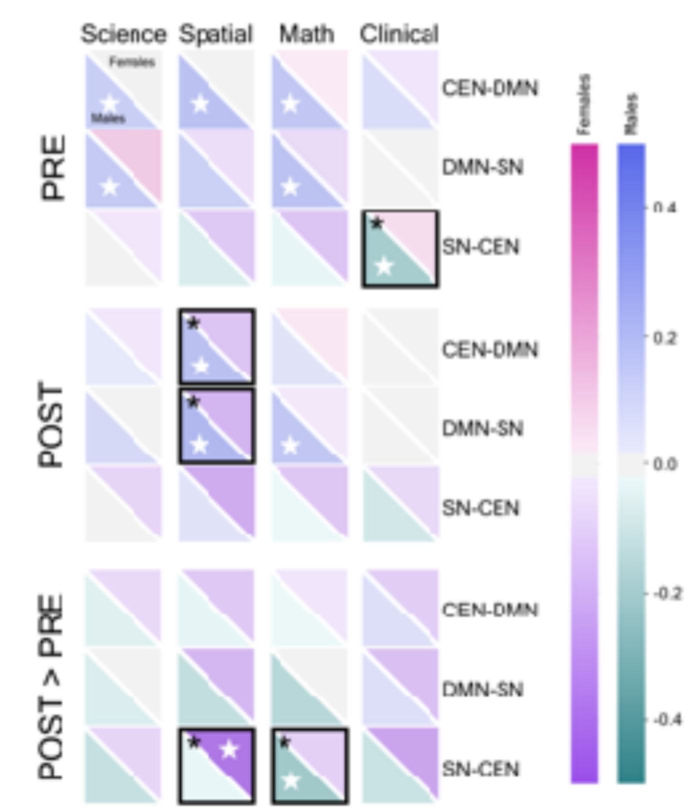
Gonzalez et al., In Revision

PREPRINT: https://doi.org/10.1101/528075

For male students,

- **Separate brain connections for STEM and clinical anxiety**
- **Fewer correlations at post**

Between-Network Correlates of Anxiety



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4. Validate a new task or data acquisition approach
5. ROI selection ✓
6. Functional decoding ✓
7. Data-driven approach to validate cognitive models ✓

Meta-Analysis Methods*

Coordinate-Based Meta-Analysis

Where do the foci converge?

Activation Likelihood Estimation (ALE)
Kernel Density Analysis (KDA)
Multilevel Kernel Density Analysis (MKDA)
Specific Coactivation Likelihood Estimation (SCALE)
Seed-Based d-Mapping
MKDA Chi2 Extension

Image-Based Meta-Analysis

Where do the images converge?

Mixed-Effects GLM (gold standard)
Fixed-Effects GLM
Fisher's IBMA
Stouffer's IBMA
z permutation

***Currently, these methods are spread out across programming languages and user interfaces**

Okay, I've convinced you… what do you do next?

Library of meta-analytic images

Browse for ideas and examples

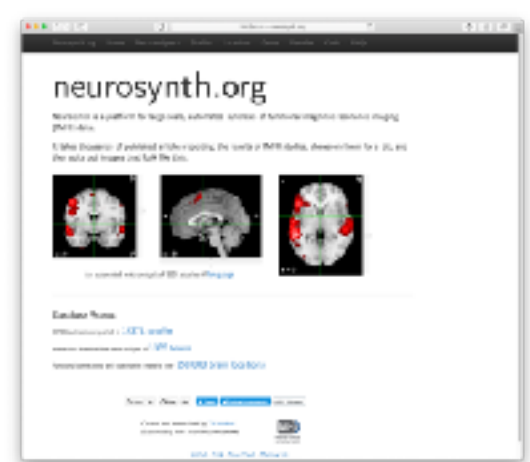
http://anima.fz-juelich.de/query

Database and software for meta-analyses

Detailed manual, paradigm-based meta-analysis

- ALE method
- Structured taxonomy terms

http://brainmap.org

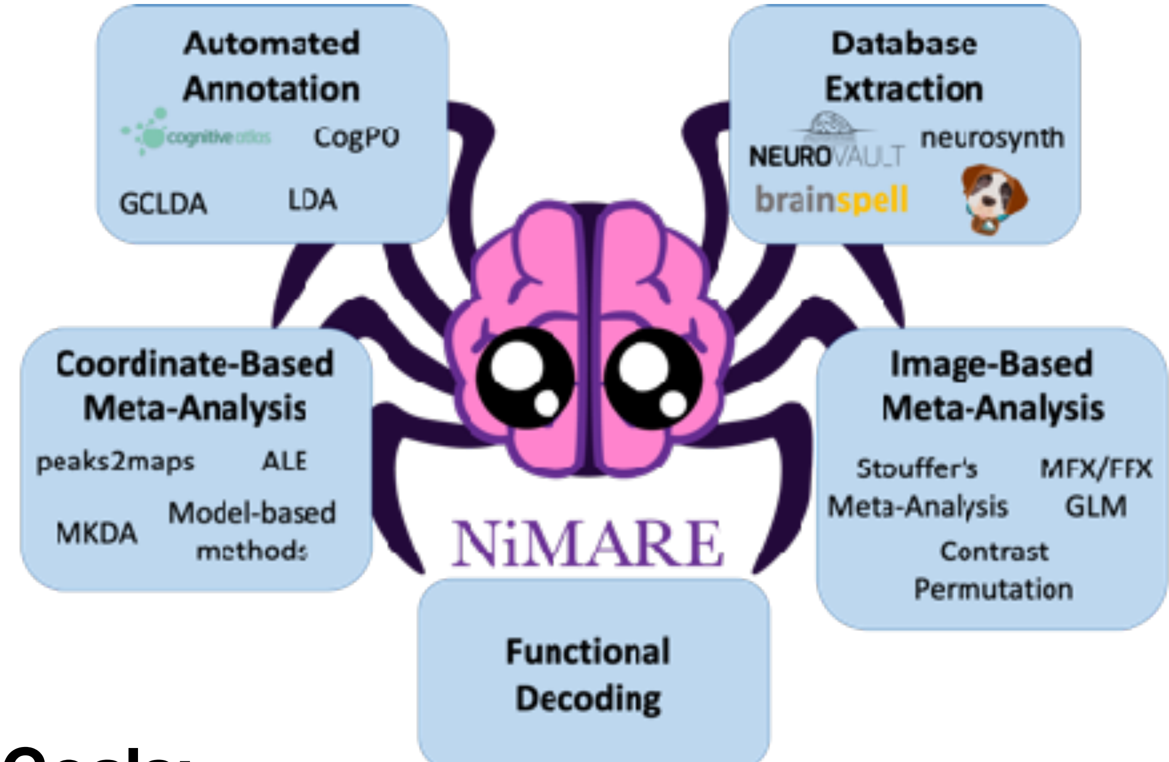


http://neurosynth.org

Automated and fast meta-analysis and decoding

- MKDA method
- Rich set of author terms

NiMARE: A *Neuroimaging Meta-Analysis Research Environment*

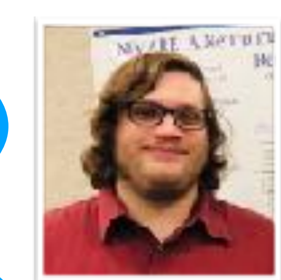


Goals:

- Implement a common interface across different meta-analysis packages that perform similar tasks
- Facilitate open source community development
- Provide a standard syntax for a variety of different analyses that interact with coordinate and image-based databases (e.g., Neurosynth, Brainspell, NeuroVault)
- Joins the Python neuroimaging ecosystem (along with nipype, nistats, and nilearn

https://github.com/neurostuff/NiMARE

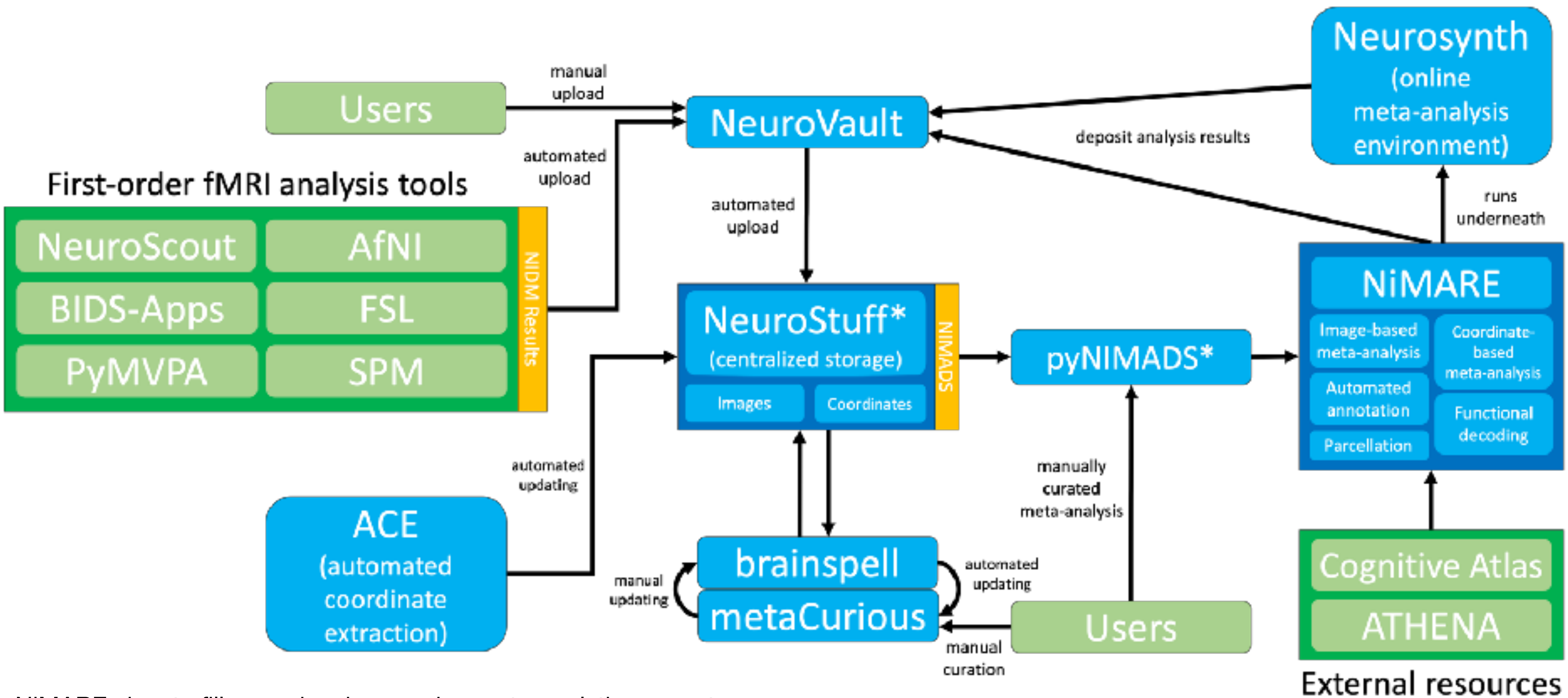
Please contribute!



Slide courtesy of Taylor Salo

NiMARE: A *Neuroimaging Meta-Analysis Research Environment*

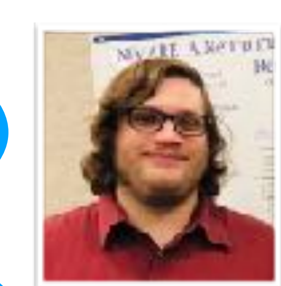
What role does NiMARE play in the broader Python ecosystem?



- NiMARE aims to fill a gap in a burgeoning meta-analytic ecosystem.
- The goal of NiMARE is to collect a wide range of meta-analytic tools in one Python library.
- Currently, those methods are spread out across a range of programming languages and user interfaces, or are never even translated from the original papers into useable tools.
- NiMARE operates on NIMADS-format datasets, which users will be able to compile by searching the NeuroStuff database with the pyNIMADS library.
- A number of other services in the ecosystem will then use NiMARE functions to perform meta-analyses, including Neurosynth 2.0, NeuroVault, and metaCurious.

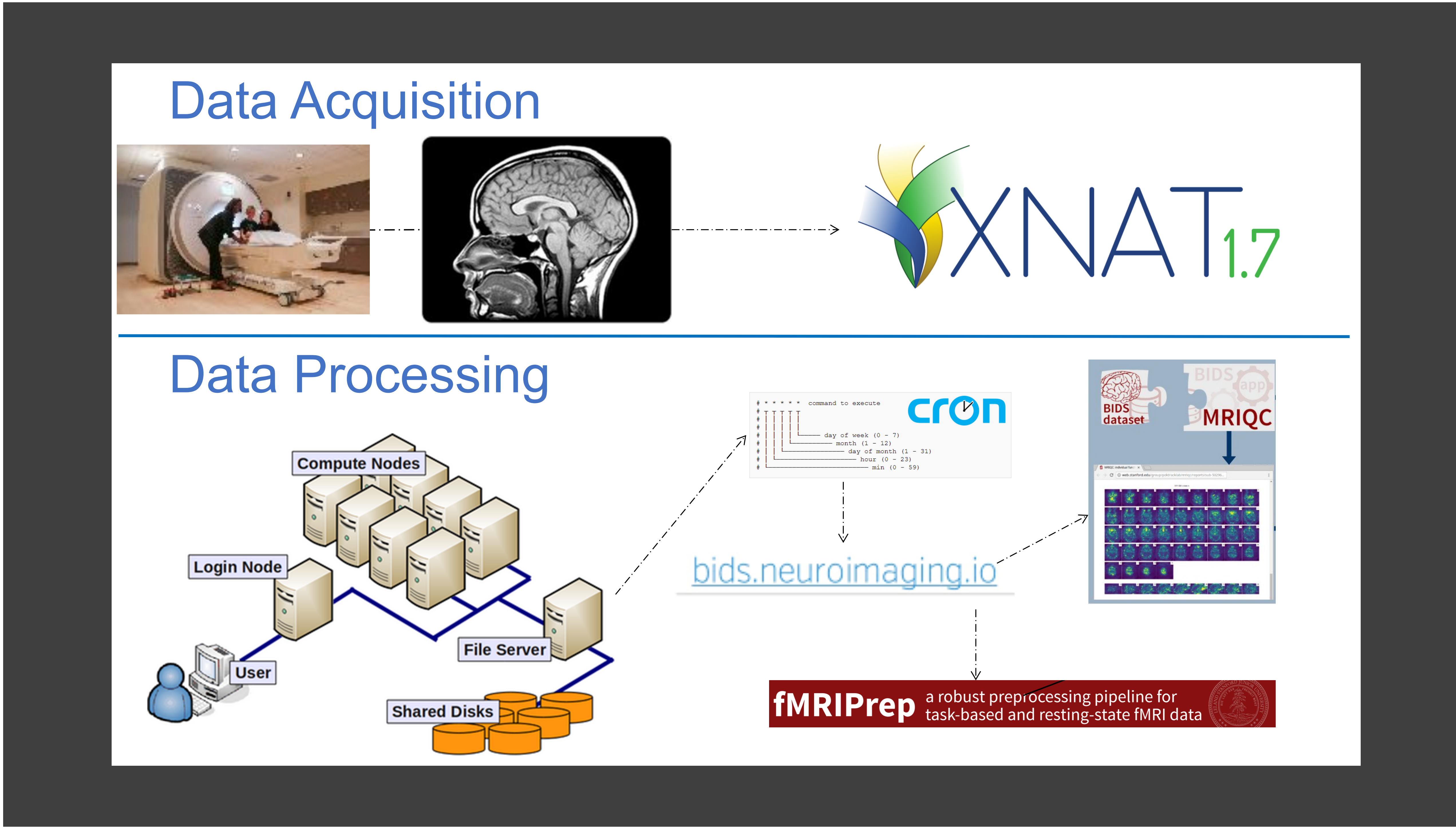
https://nimare.readthedocs.io/en/latest/about.html

Please contribute!



Slide courtesy of Taylor Salo

Our lab's best practices for **Open Science** and **Reproducible Neuroimaging**



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Our lab's best practices for **Open Science** and **Reproducible Neuroimaging**

Data and Software Resources

- **OpenNeuro:** hosts open-source datasets
- **Neurovault:** hosts statistical maps
- **ANIMA:** hosts meta-analysis maps
- **Neurosynth:** coordinate-based database
- **Nipy:** community of practice devoted to use of Python*
- **Github:** code hosting for collaboration and version control
- **NITRC**: software clearinghouse and repository

Community Resources

- **NeuroStars:** neuroinformatics forum run by INCF
- **Brainhack Slack:** collaborative workshops
- **Listservs & Slack**
- **ReproNim:** "*Discover, Describe, Do*"

***nipype, dipy, mindboggle, nibabel, Scitran SDM, Nipy, Nitime, popeye, Nilearn, PyMVPA, MNE, niwidgets**

- **nipype: provides an interface to existing software**
- **nibabel: read/write common file formats**
- **Nilearn: uses scikit-learn for statistical learning**

NEUROVAULT

OpenNEURO

Slide courtesy of Katie Bottenhorn

Our lab's best practices for **Open Science** and **Reproducible Neuroimaging**

GitHub: code hosting platform

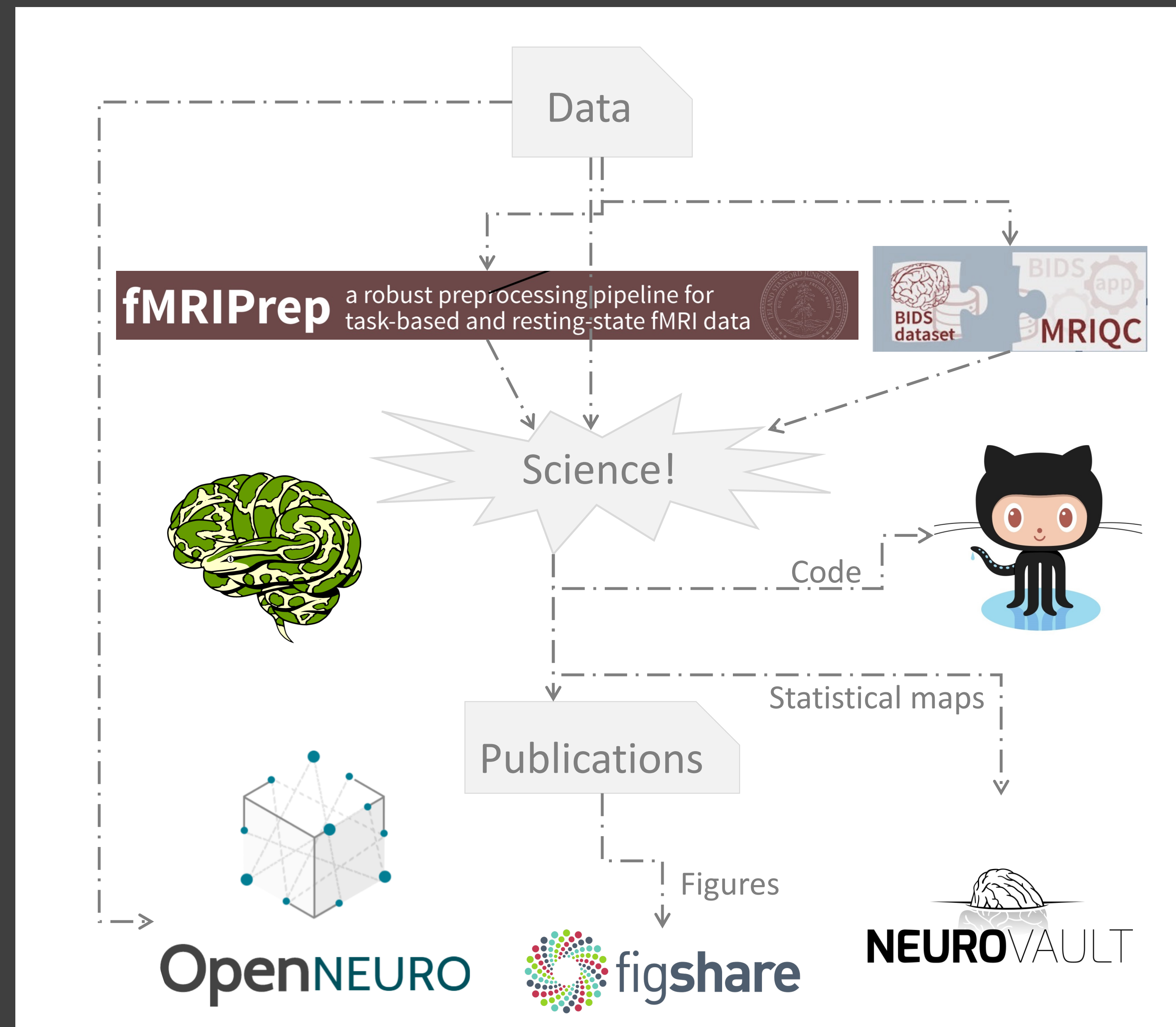
- **Version Control**
  - Track changes in code to revert mistakes and record logic
- **Sharing Methods**
  - Link code in papers to improve reproducibility
  - Integration with interactive notebook tools
- **Collaboration**
  - Other users can contribute through pull requests
  - Search tools improve discoverability

Slide courtesy of Taylor Salo

Our lab's best practices for **Open Science** and **Reproducible Neuroimaging**

Analyses and Sharing

1. **Use open-source, BIDS-friendly tools**
   - fMRIPrep
   - MRIQC
   - Nipy
   - Github
2. **Share your code & results**
   - Code on GitHub
   - Maps to NeuroVault
   - Figures to figshare
   - Reference in your paper!
3. **Share your data on OpenNeuro**
   - Share with the community
   - Citable datasets (data papers)



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Our lab's best practices for **Open Science** and **Reproducible Neuroimaging**

Analyses and Manuscripts

Preregistration: Design analysis plan prior to data acquisition
- Separate confirmatory and exploratory analyses
- Prevent HARKing, p-hacking, etc.

Open Science Framework

Registered Report: Submit manuscript prior to data acquisition
- Same benefits as above
- Plus peer-reviewed analysis plan

Preprint: Share manuscripts openly prior to peer review
- Crowdsourced peer review
- Early access to research findings
- Open access

bioRxiv THE PREPRINT SERVER FOR BIOLOGY

PsyArXiv

arXiv.org

OSF

CENTER FOR OPEN SCIENCE

aims to increase openness, integrity, and reproducibility of research

OPEN DATA OPEN MATERIALS PREREGISTERED

Slide courtesy of Taylor Salo

Our lab's best practices for **Open Science** and **Reproducible Neuroimaging**

Sharing Other Study Materials

- **Analysis Plans**
- **Figures**
- **Posters**
- **Talks**
- **Tasks and Stimuli**

OSF includes tools for collaboration, registration, and integrations for storage tools like Figshare, GitHub, and Google Drive. OSF projects can be kept private until publication in order to prevent scooping.

figshare provides DOIs for stored objects, like figures or data (but not neuroimaging data).

Zenodo integrates with GitHub to allow you to assign citable DOIs to versioned releases of your code. DataCite is working with Zenodo to track code citations, and can be integrated with ORCID very easily.

Slide courtesy of Taylor Salo

Before we go…

Academia is very hierarchical
And power differentials always create space for the abuse of power
This is true regardless of gender, sexual, racial/ethnic, or cultural identity

Lots of advice is well-intentioned but pretty terrible

Tell someone. Report the abuse. Inaction. Retaliation. Career suicide.

It'll get better… I survived and so can you. Deal with it?

Find a community of support. This isn't the victims' problem to fix/cope/manage.

A toxic climate hurts <u>everyone</u>. What can we collectively do?

Listen. Don't interrupt. Prevent others from interrupting.

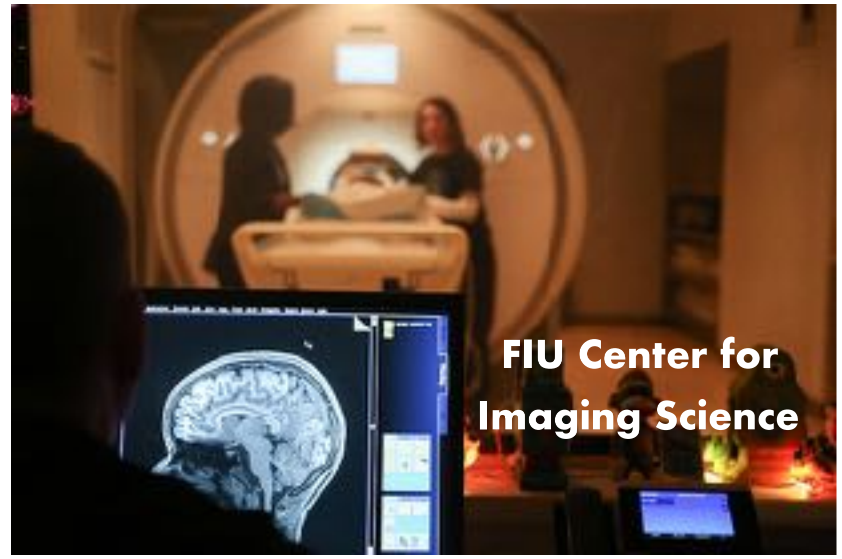
Seek out other perspectives. Twitter is a hell site, but go find the voices you can learn from. Follow LGBTQ+, Black, Latinx, Muslim scientists, scholars, and activists

Change your surroundings, situate yourself as an Other. Look at your collaborators. We naturally seek out "like-minded people" but this can create our own scientific echo chambers. Rich and innovative ideas are cultivated in a diverse and inclusive environment.

Florida International University, Miami, FL, USA

FIU is an urban, multi-campus, public research university serving its students and the diverse population of South Florida.

57,000	Students Enrolled
FOURTH	Largest University in USA
DIVERSE	61% Hispanic, 15% White Non-Hispanic, 13% Black, 4% API, 7% Other
SECOND	Highest Number of Bachelor and Master's Degrees to Latinxs in STEM



Thank You!

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