# How can fMRI inform the structure of the mind?

Russell Poldrack

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Do we really know an order of magnitude more now than we did in 2002?



Do we really know an order of magnitude more now than we did in 2002?

Will 45,000 more of the same kind of fMRI papers give us twice the understanding we have now?

# Questions we would hope we could answer

- What does <insert brain area or system> do?
- How is <insert psychological process> implemented in the brain?

# What does the anterior cingulate cortex do?

- "anterior cingulate" and fMRI
  - 3683 abstracts in PubMed
  - under conservative assumptions, ~\$22M USD

# What does the ACC do?

### maintenance



### pain



### phonology



### interference



# difficulty

### conflict

### errors

### attention









forward inference Z estimated using neurosynth.org

# playing 20 questions with nature is a bad strategy

YOU CAN'T PLAY 20 QUESTIONS WITH NATURE AND WIN: PROJECTIVE COMMENTS ON THE PAPERS OF THIS SYMPOSIUM

> Allen Newell May, 1973



I am distressed. I can illustrate it by the way I was going to start my comments, though I could not in fact bring myself to do so. I was going to draw a line on the blackboard and, picking one of the speakers of the day at random, note on the line the time at which he got his PhD and the current time (in mid-career). Then, taking his total production of papers like those in the present symposium, I was going to compute a rate of productivity of such excellent work.. Moving, finally, to the date of my chosen target's retirement, I was going to compute the total future addition of such papers to the (putative) end of this man's scientific career. Then I was going to pose, in my role as discussant, a question: Suppose you had all those additional papers, just like those of today (except being on new aspects of the problem), where will psychology then be? Will we have achieved a science of man adequate in power and commensurate with his complexity? And if so, how will this have happened via these papers that I have just granted you?

# Establishing selective inference



Establishes a selective association between mental states/processes and brain activity

Poldrack & Yarkoni, 2016, Annual Review in Psychology

# Decoding tasks from fMRI

#### **PSYCHOLOGICAL SCIENCE**

#### **Research** Article

#### Decoding the Large-Scale Structure of Brain Function by Classifying Mental States Across Individuals

Russell A. Poldrack,<sup>1</sup> Yaroslav O. Halchenko,<sup>2</sup> and Stephen José Hanson<sup>3</sup>

<sup>1</sup>University of California, Los Angeles; <sup>2</sup>Dartmouth University; and <sup>3</sup>Rutgers University

#### 8 tasks, 130 individuals

#### Task chosen by classfier Task 2 Task 3 Task 1 Task 4 Task 5 Task 7 Task 6 87.5 6.0 0.0 0.0 6.0 0.0 0.0 90.0 0.0 5.0 0.0 0.0 0.0 0.0 8.0 23.0 61.5 0.0 8.0 0.0 0.0

82.4

0.0

0.0

0.0

0.0

0.0

43.8

0.0

0.0

0.0

0.0

18.2

71.4

0.0

0.0

#### 26 tasks, 338 individuals

#### frontiers in NEUROINFORMATICS



Task I

Task 2

Task 3

Task 4

Task 5

Task 6

Task 7

Task 8

0.0

0.0

0.0

0.0

0.0

0.0

38.0

28.0

11.0

0.0

0.0

0.0

0.0

0.0

7.0

task

True

#### Toward open sharing of task-based fMRI data: the OpenfMRI project

Russell A. Poldrack<sup>1</sup>\*, Deanna M. Barch<sup>2</sup>, Jason P. Mitchell<sup>3</sup>, Tor D. Wager<sup>4</sup>, Anthony D. Wagner<sup>5</sup>, Joseph T. Devlin<sup>6</sup>, Chad Cumba<sup>1</sup>, Oluwasanmi Koyejo<sup>7</sup> and Michael P. Milham<sup>8</sup>



#### poldracklab.org

Task 8

0.0

5.0

0.0

18.0

0.0

0.0

5.0

63.0

0.0

0.0

0.0

84.0

27.0

- It's not tasks we ultimately want to decode
  - It's cognitive processes/states/functions
  - First we need to know what those are!





• What are all the enzymes?





What are all the psychological functions that we are mapping to the brain?









# Task decompositions

	<u>Task Pair I</u>		Task Pair II			Task Pair III			Task Pair IV		
	Words		Letters			Objects		Colours			
Tasks:	A	В	A	В		A	В		A	В	
	1	2	3	4		5	6		7	8	
Cognitive Processes											
Form processing					Ì						
Colour processing					ł						
Lexical orthography									_	_	
Sublexical orthography											
Object structure											
Semantics											
Phonology											
Articulation											

Price & Friston, 1997

# **Cognitive atlas**

a collaborative knowledge base characterizing the state of current thought in Cognitive Science.

CONCEPTS / 802

**TASKS / 707** 

**DISORDERS / 217** 

COLLECTIONS / 41

### Welcome to Cognitive Atlas

The Cognitive Atlas is a collaborative knowledge building project that aims to develop a knowledge base (or ontology) that characterizes the state of current thought in cognitive science. The project is led by Russell Poldrack, Professor of Psychology at Stanford University. Development of the project was supported by grant RO1MH082795 from the National Institute of Mental Health.

Registered users may	edit and con	tribute to the
Jognitive Atlas		
your email addre	SS	
Keep me logged i	n 🗆	SIGN I
1000 110 109900 1	Forgotte	n password
Request	a contribu	utor accourt

ABOUT

BLOG

Recently updated mental CONCEPTS

- kindness priming
- auditory recognition

Recently updated experimental TASKS

 Multidimensional Personality Questionnaire Recently updated **DISORDERS** 

Semantic Dementia

surface dyslexia

Recently updated COLLECTIONS

 NCANDA Speed - General Ability

Poldrack et al., 2011, Frontiers in Neuroinformatics



#### Poldrack et al., 2011, Frontiers in Neuroinformatics

# Ultimate goal: ontology-enabled meta-analysis



# Where will the data come from?



Poldrack & Gorgolewski, 2014

# Sharing statistical maps: neurovault.org

NeuroVault Collections - FAQ Give feedback

Q Log in



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!

# Cognitive Atlas annotation of neurovault data



### Does image similarity relate to ontological similarity?



Wang et al., 2007, Bioinformatics; Sochat et al., 2015, Frontiers in Brain Imaging Methods

# Ontological similarity and image similarity





Sochat et al., in prep

# Voxelwise encoding model for cognitive processes



Voxel response (Z-score) for each task contrast Ontology encoding for each task contrast (expanded to include all parent terms)

Weighting for each ontology element

Estimate  $\beta$  using regularized regression (elastic net)

#### cognitive processes



Х

# Predicting activation maps from cognitive processes



# Predicting activation maps from cognitive processes



Term accuracy (for terms with 10+ images)

response execution	0.95	48
visual object recognition	0.95	11
object recognition	0.93	12
working memory maintenance	0.93	12
decision making	0.92	18
response selection	0.91	45
visual recognition	0.90	52
recognition	0.89	58
memory	0.89	58
visual perception	0.88	56
form perception	0.86	34
visual form recognition	0.86	33
maintenance	0.86	15
perception	0.85	62
proactive control	0.83	10
visual word recognition	0.80	12
word recognition	0.80	12
detection	0.78	12
updating	0.78	14
cognitive control	0.77	27
auditory perception	0.74	10
	-	

Sochat et al., in prep

# Selective inference: Summary

- Ontology-based meta-analysis provides basis for prediction of maps based on cognitive processes
- To advance we need:
  - More data
  - Better annotated data
  - A better ontology?
    - How would we know if ours is wrong?

















#### Franz Yarkoni

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Apple	iCloud	Yahoo	Bing	Google	Wikipedia	Faceboo	k Twitter	LinkedIn	The Weathe	r Channel	Yelp	pubmed
				Home	Meta-ana	ilyses -	Studies	Locations	Decoder	Code	FAQs	Sign in

### phrenosynth.org

Phrenosynth is a platform for large-scale, automated synthesis of functional magnetic resonance imaging (fMRI) data.

It takes thousands of published articles reporting the results of fMRI studies, chews on them for a bit, and then spits out images like this:





An automated meta-analysis of 885 studies of SUAVITY



g

# "Multiple demand" areas: Phrenosynth

### benevolence





mirth

# ideality



# sublimity



### conjugal love fi

### firmness

### human nature

### suavity








- Activation imaging may not tell us whether our current ontology is wrong
  - Or maybe it already is telling us that!
- What reason do we have to think that our ontology might be wrong or incomplete?

## Hop in the time machine...

MONTH	DAY	YEAR	HOUR	MIN		
	88			88		
DESTINATION TIME						
MONTH	DAY	YEAR	HOUR	MIN		
		2015				
PRESENT TIME						
MONTH	DAY	YEAR	HOUR	MIN		
	88	BBBB		88		
00	LA	ST TIME DEPAR	TED			

- Chemistry:
  - Intense debate over the atomic theory
  - Ernst Mach (1897): ""I don't believe that atoms exist!"
  - not settled until Einstein (1905)



John Dalton (credit: <u>wikipedia.org</u>)



- Biology
  - Cell theory (proposed in 1839) and germ theory of disease (1860's) finally accepted by most biologists
  - Heredity not understood
    - Mendel's work would not be rediscovered for 10 more years





- Computer science
  - Hollerith's mechanical "tabulating machine" used by US Census for first time
  - General-purpose programming languages would not appear for 50 more years



credit: wikipedia.org



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- Neuroscience
  - Ramon y Cajal (1888) provides first evidence for neuron doctrine over the reticular theory



#### The 1890's in science

- Psychology
  - William James' Principles of Psychology



AMERICAN SCIENCE SERIES-ADVANCED COURSE THE PRINCIPLES OF PSYCHOLOGY BY. WILLIAM JAMES PROFESSOR OF PSYCHOLOGY IN HARVARD UNIVERSITY IN TWO VOLUMES VOL. I NEW YORK HENRY HOLT AND COMPANY 1890

## Topic headings from James, 1890

- "To How Many Things Can We Attend At Once?"
- "The Varieties Of Attention."
- "The Improvement Of Discrimination By Practice"
- "The Perception Of Time."
- "Accuracy Of Our Estimate Of Short Durations"
- "To What Cerebral Process Is The Sense Of Time Due?"
- "Forgetting."
- "The Neural Process Which Underlies Imagination"
- "Is Perception Unconscious Inference?"
- "How The Blind Perceive Space."
- "Emotion Follows Upon The Bodily Expression In The Coarser Emotions At Least."
- "No Special Brain-Centres For Emotion"
- "Action After Deliberation"

## What does a conceptual revolution look like?

- Gene Ontology
  - A formal description of concepts in biology and their relations
    - biological processes (28,566)
      - MAPK cascade *is-a-kind-of* intracellular signal transduction
      - signal transduction *is-a-part-of* cell communication
    - molecular functions (10,057)
      - RNA polymerase II core binding *is-a-kind-of* protein complex binding
    - cellular components (3,903)
      - endoplasmic reticulum *is-a-kind-of* cytoplasmic part
      - Golgi apparatus *is-a-part-of* endomembrane system



from QuickGO: http://www.ebi.ac.uk/QuickGO/

#### 1890's biology textbooks



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## Linguistic evidence for conceptual revolution

 What proportion of Gene Ontology terms are mentioned in these books?

	Huxley	Parker	Overlap
biological process (28,566)	0.09% (26)	0.1% (32)	20
molecular function (10,057)	0 (0)	0 (0)	
cellular component (3,903)	1.05% (41)	1.01% (40)	25

#### How much conceptual progress has psychology made?

- 22.9% of all Cognitive Atlas mental concepts are used at least once in James' Principles of Psychology
- Examples:
  - goal, deductive reasoning, effort, false memory, object perception, visual attention, task set, anxiety, mental imagery, unconscious perception, internal speech, primary memory, theory of mind, judgment



## A broader view: Folk usage of ontology terms

- Analyzed Google N-Gram corpus (3.38 million books) for term mentions from 1800-2000
- Separated by phrase length
  - Random sample from GO terms

#### Google Books Ngram Viewer



#### Many psychological concepts are linguistically ancient

Cognitive Atlas concepts



#### Many psychological concepts are linguistically ancient

1800

1850



#### **GO Molecular Functions**





1900

Years

1950

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2000

- We would hope that our psychological ontology would align with data from neuroscience
- How can we test this?













Observed covariance





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#### How confident are we in our scientific approach?



A HINT TO PHRENOLOGISTS; or, "September 20, 1878."

#### How confident are we in our scientific approach?



A HINT TO PHRENOLOGISTS; or, "September 20, 1878."

#### Science in crisis (?)



IN THE WAKE OF HIGH-PROFILE CONTROVERSIES, PSYCHOLOGISTS Are facing up to problems with replication.

BY ED YONG



## Raise standards for preclinical cancer research

C. Glenn Begley and Lee M. Ellis propose how methods, publications and incentives must change if patients are to benefit.

29 MARCH 2012 | VOL 483 | NATURE | 531



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#### Neuroimaging: a perfect storm for irreproducibility



Stanford Center For Reproducible Neuroscience



#### **Reproducibility matters**

Neuroscience research is the basis for critical decisions about health and society. Our first goal as researchers is to ensure that the results of our research will stand the test of time.

#### **Enabling better research**

We are expanding the OpenfMRI project into a free and open platform that will enable the analysis and sharing of neuroimaging data, harnessing the power of high-performance computing to improve the quality of research.

#### From data to discovery

Our platform will provide neuroimaging researchers with leading-edge tools to analyze and share large datasets, with a focus on quantifying the reproducibility of the results.

#### http://reproducibility.stanford.edu

#### Designing a more reproducible scientific enterprise



#### Designing a more reproducible scientific enterprise





## Improving the choice architecture of science

- Choice architecture
  - particular set of features that drive people toward or away from particular choices
- Nudges
  - Improving incentives
  - Using the power of defaults
  - Providing feedback
  - Expecting and prevent errors



Improving Decisions about Health. Wealth. and Happiness Richard H. Thaler and Cass R. Sunstein ...with a new afterword

"One of the few books I've read recently that fundamentally changes the way I think about the world." --Steven Levitt, coauthor of Freakmonian

#### Threats to reproducibility: Low power

# Power failure: why small sample size undermines the reliability of neuroscience

Katherine S. Button<sup>1,2</sup>, John P. A. Ioannidis<sup>3</sup>, Claire Mokrysz<sup>1</sup>, Brian A. Nosek<sup>4</sup>, Jonathan Flint<sup>5</sup>, Emma S. J. Robinson<sup>6</sup> and Marcus R. Munafõ<sup>1</sup>



#### Sample size and power in fMRI studies



Median estimated sample size in 2015 = 43Median effect size with 80% power = 0.61

Thanks to Sean David and Tal Yarkoni for sample size data

Poldrack et al, submitted

#### What are realistic effect sizes for fMRI?



Estimated from HCP task data using combined anatomical + neurosynth ROIs

Poldrack et al, submitted
#### Low power -> unreliable science

Positive Predictive Value (PPV): The probability that a positive result is true

Winner's Curse: overestimation of effect sizes for significant results

 $PPV = ([1 - \beta] \times R) / ([1 - \beta] \times R + \alpha)$ 



Button et al., 2013

 "My result isn't significant, so I need to add more subjects..."

## Sample size flexibility



**Fig. 1.** Likelihood of obtaining a false-positive result when data collection ends upon obtaining significance ( $p \le .05$ , highlighted by the dotted line). The figure depicts likelihoods for two minimum sample sizes, as a function of the frequency with which significance tests are performed.

-Simmons et al., 2011, Psychological Science

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#### Improvement: always predetermine sample size

#### neuropowertools.org

#### NeuroPower



control at level 0.05, the minimal sample size is 40.

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Joke Durnez

### Threats to reproducibility: Methodological flexibility

- Using standard FSL analysis options
  - 69,120 possible analysis workflows

Processing step	Reason	Options	Number of plausible options
Motion correction	Correct for head motion during scanning	Interpolation [linear vs. sinc] Reference volume [single vs. mean]	4
Slice timing correction	Correct for differences in acquisition timing of different slices	No/before motion correction/after motion correction	3
Field map correction	Correct for distortion due to magnetic susceptibility	Yes/No	2
Spatial smoothing	Increase SNR for larger activations and ensure assumptions of Gaussian random field theory	FWHM [4/6/8 mm]	3
Spatial normalization	Warp individual brain to match a group template	Method [linear/nonlinear]	2
High pass filter	Remove low-frequency nuisance signals from data	Frequency cutoff [100, 120]	2
Head motion regressors	Remove remaining signals due to head motion via statistical model	Yes/No If Yes: 6/12/24 parameters or single timepoint "scrubbing" regressors	5
Hemodynamic response	Account for delayed nature of hemodynamic response to neuronal activity	Basis function [single- gamma, double-gamma] Derivatives [none/shift/dispersion]	6
Temporal autocorrelation model	Model for the temporal autocorrelation inherent in fMRI signals.	Yes/no	2
Multiple comparison correction	Correct for large number of comparisons across the brain	Voxel-based GRF, Cluster- based GRF, FDR, nonparameteric	4
Total possible workflows			69,120

#### Threats to reproducibility: Methodological flexibility

frontiers in <b>DRIGINAL RESEARCH ARTICLE</b> published: 11 October 2012 doi: 10.3389/fnins.2012.00149	
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# On the plurality of (methodological) worlds: estimating the analytic flexibility of fMRI experiments

Joshua Carp\*

6,912 pipelines



## Multiple comparison correction

- Assessed latest 100 papers matching query for fMRI activation studies
  - 65 reported whole-brain activation data
  - Good news
    - only 3 papers reported uncorrected results
  - Bad news
    - 11% of papers analyzed data using SPM/FSL but then corrected for multiple comparisons using AFNI's alphasim/3dclustsim
    - Why is this a problem?

Poldrack et al., submitted

## Communal p-hacking?

- Eklund et al. (2016, PNAS)
  - "a 15 year old bug was found in 3dClustSim while testing the three software packages (the bug was fixed by the AFNI group as of May 2015, during preparation of this manuscript). The effect of the bug was an underestimation of how likely it is to find a cluster of a certain size (in other words, the pvalues reported by 3dClustSim were too low)."
  - AFNI also underestimated smoothness



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# The garden of forking paths

The garden of forking paths: Why multiple comparisons can be a problem, even when there is no "fishing expedition" or "p-hacking" and the research hypothesis was posited ahead of time\*

> Andrew Gelman<sup>†</sup> and Eric Loken<sup>‡</sup> 14 Nov 2013



# The garden of forking paths

The garden of forking paths: Why multiple comparisons can be a problem, even when there is no "fishing expedition" or "p-hacking" and the research hypothesis was posited ahead of time\*

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## Improvement: Study pre-registration

- Register sample size and analysis plan up front
- This does not prevent exploratory analysis
  - But planned and exploratory analyses must be clearly delineated in the paper

## Improvement: Mapping the garden



Tracking every analysis allows a full characterization of exploration

### Improvement: Quantifying "vibration of effects"



Focusing on finding generalizable results, rather than hitting the p<0.05 jackpot

## Study reporting and transparency

- In 22 of the 65 papers we analyzed for multiple comparison procedures, it was impossible to identify precisely which correction technique was used
  - beyond generic terms such as "cluster based correction"

### Improvement: Better study description

- OHBM Committee on Best Practices in Data Analysis and Sharing (COBIDAS) report
  - <u>www.humanbrainmapping.org/cobidas/</u>
- In the future, tools may be able to automatically generate standards-compliant methods text from a nipype workflow

## Improvement: Sharing of analysis platforms

- "an article about a computational result is advertising, not scholarship. The actual scholarship is the full software environment, code and data, that produced the result." - Buckheit & Donoho, 1995
- The tale of myconnectome

### Virtual machines as tools for reproducible science





## Conclusions

- fMRI has come a long way in 20 years, but we have a long way to go
- We need to move towards approaches that will give us greater insight into selective mind-brain mappings
- "The first principle is that you must not fool yourself and you are the easiest person to fool"
  - R. Feynman
  - We need to redesign the choice architecture of fMRI methods so that it prevents rather than affords fooling ourselves

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National Institute on Drug Abuse



James S. McDonnell Foundation

#### The Poldrack Lab @ Stanford

http://reproducibility.stanford.edu



Data sets and code will be made available at <u>www.openfmri.org</u>

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